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The
Medical Clinics of Chicago

VOLUME 2 NUMBER 2

CLINIC OF DR. CHARLES SPENCER WILLIAMSON

COOK COUNTY HOSPITAL

A CASE OF ACUTE MILIARY TUBERCULOSIS

Striking Similarity to Typhoid Fever. Positive Widal Reaction on Repeated Examinations, Subsequently Becoming Negative. Onset with a Chill. Progressive Leukopenia. Relatively Rapid Pulse and Respirations. Development of Fine Rales Throughout the Lung a Few Days Before Death. Autopsy Findings.

THE patient whom I want to show you today is a colored man, thirty-two years of age, with a somewhat unusual occupation for his race, that of a tailor. He entered the hospital on June 8th with the examining-room diagnosis of a rheumatic infection. His complaints were three in number: First, a severe chill; second, painful and frequent urination; third, fever.

Onset and Course.—The patient states that two weeks ago, after having worked hard all day, he developed a marked chilly sensation which lasted, he thinks, for a full hour. From his description this seems to have been a genuine chill. In any event, he went to bed and the next day woke up with a headache. Just a week after this he commenced to notice some difficulty or, more properly speaking, some pain on urination, having to pass urine every three or four hours. During this period he remained in bed most of the time and thinks he had fever all the time. He has had no pain in the chest or abdomen and no nosebleed. His bowels have been regular and at no time has he had

any diarrhea. He has not been short of breath and really came into the hospital because of the fever.

Past History.—He had malaria fourteen years ago and has had many attacks of sore throat, none of them, however, of special severity.

Family History.—He is married, his wife is living and well; she has had one miscarriage, but no children. His father and mother died of pneumonia and old age respectively. He had no brothers or sisters. His venereal history is negative as regards lues, but he admits having had gonorrhea ten years ago which became chronic and resulted in a stricture five years ago, which is still in existence.

Habits.—He does not use alcoholics and uses tobacco moderately. His bowels have always been regular. Up to the past few weeks his appetite has been poor. He thinks he has lost weight.

Physical Examination (on Admittance).—The patient is a poorly nourished negro who looks acutely and seriously ill.

Head and Neck.—The pupils are sluggish, medium wide, and react to light and accommodation. The mouth shows marked pyorrhea and a heavily coated tongue, yellowish in color, with red tip and edges. The neck shows one or two moderately enlarged glands. The ears, nose, and scalp are negative.

The *thorax* is symmetric; expansion is equal on both sides and excursion is good. The lungs are entirely negative. No râles can be heard and no areas of dulness can be made out. In particular, nothing abnormal was elicited at the apices.

The heart.—The apex-beat is in the fifth interspace; no murmurs and no thrills can be heard. The heart sounds are rapid, ranging from 114 to 130.

This examination was made on the morning following his admission, at a time, as you will see from the temperature-curve, when he had developed considerable fever.

The *abdomen* is a little bit tense, but not definitely rigid. The liver dulness shows nothing special; the liver is not palpable. There is a little tenderness in the suprapubic region.

The spleen cannot be palpated, nor is the splenic dulness increased. The genitalia are negative.

The *extremities* show nothing abnormal. The reflexes are all normal.

Rectal examination discloses a firm, hard, moderately enlarged prostate.

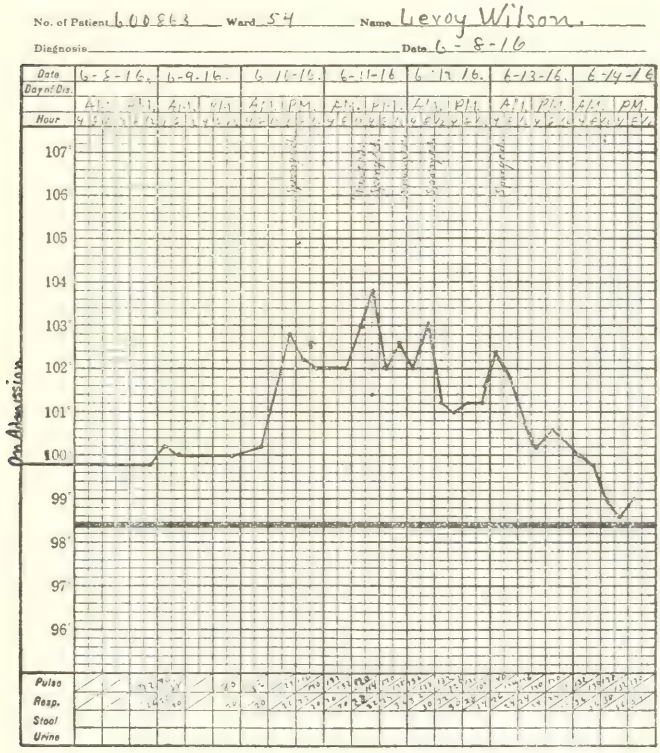

Fig. 42.—Temperature chart in a case of acute miliary tuberculosis.

The blood-pressure is 110 systolic, 80 diastolic.

As you will see by reference to the temperature-curve, he had little fever, 99.8° F., on entrance, with a pulse of 72 and respirations of 20. The following day the temperature remained about the same, 100° F. all day. On the next day the temperature rose in the afternoon to 102.8° F., the pulse jumping

up to 124, the respirations remaining in the neighborhood of 20, and from that time on his pulse has ranged from 120 to 130.

Now when we examine this history we see that it is characterized very largely by its negative findings. There is substantially nothing to attract our attention to any particular organ unless it be the pain and frequent urination, directing attention to the bladder. It is very evident that the patient has some sort of an infection. The chill, rising temperature, and general prostration all indicate this with considerable certainty, but where this infection may be, and of what nature, is certainly not clear from the history alone.

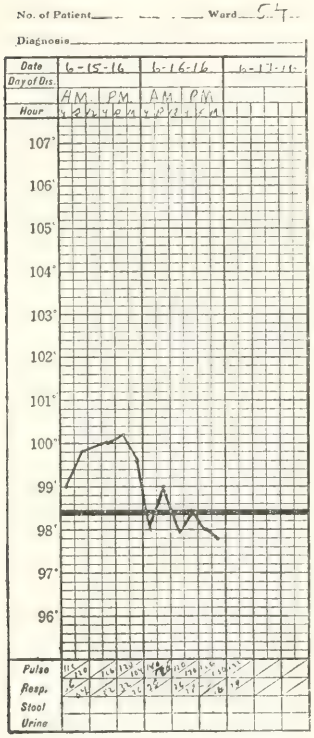

Fig. 43.—Temperature chart in a case of acute miliary tuberculosis.

Because of the pain and frequency of urination we made a *urinalysis* immediately and found an amber-colored specimen with a specific gravity of 1020, acid in reaction, a mere trace of albumin, no sugar, an occasional erythrocyte, one or two hyaline casts, and a small amount of pus in a centrifuged specimen. A diazo-reaction was made and was strongly positive, one of the most positive reactions of this sort which I have seen for some time. A twenty-four-hour specimen was then collected, which showed a specific gravity of 1030 with an amount of 250 c.c., a mere trace of albumin, and a few pus-cells. An attempt to catheterize the patient was unsuccessful because of a tight stricture. After such disinfection of the meatus as was possible a specimen was obtained and examined for tubercle bacilli. Quite a large number of acid-fast organisms were found in this

specimen, but the morphology was not quite that of tubercle bacilli, and it was concluded that they were probably due to contamination. The following day an attempt was made to cultivate the organism from the urine, but nothing was found except some Gram-positive cocci resembling staphylococci. No typhoid or colon bacilli were found.

The *blood examination* was made the day after admission and showed 10,000 leukocytes and 98 per cent. hemoglobin. The differential count showed 68 per cent. polymorphonuclear neutrophils, 30 per cent. small lymphocytes, 1 per cent. large mononuclears, and an occasional myelocyte. *The Widal reaction was strongly positive in a dilution of 1 : 40.* A Wassermann on the blood was also made and was negative. A blood-culture was negative for typhoid bacilli.

We have to ask ourselves, in view of the strongly positive Widal, whether we are justified in diagnosing typhoid. There are several very peculiar things about this case which do not fit in with an average case of typhoid. On the other hand, typhoid fever is a disease with so many variations as to make it quite possible that this is typhoid. If we analyze the history we find that the disease started two weeks before the patient's entrance to the hospital with a chill, or at least chilly sensations sufficient to make him go to bed. This incubation period of two weeks would fit in very well with the incubation period of typhoid. His temperature since coming into the hospital has been steadily rising. Beginning with 99.8° F. on admission, it has gone up steadily until it is now in the neighborhood of 103° F.

If, then, this is a typhoid fever, this would probably represent the fourth or fifth day, at the most, of the actual disease, if we interpret the two weeks at home as having been the incubation period. Of course, if we assume that he had fever before coming in, it would be still later. In our experience we do not, as a rule, find so pronounced a Widal reaction on the fifth day, but exceptionally it does occur.

The thing that strikes our attention, however, is the rapidity of the pulse. In typhoid fever with a temperature of 103° F.

we generally expect a pulse ranging around 90 to 95, whereas in this patient we find a pulse of 124 with a temperature of 102.8° F., and at another time a pulse of 128 with a temperature of 102.6° F. Today I examined this patient again with great care, and was unable to detect anything different in the physical examination than was found in the original examination, except that the spleen is now just palpable. There is absolutely nothing abnormal to be heard over the heart, and a careful and painstaking examination of the lungs has not revealed a râle anywhere.

Further analysis shows us that his respirations are a little faster than we generally expect in a case of typhoid, ranging from 20 on the day of admission up to 30 or 32 when his temperature has been around 102° and 103° F. The rapidity of the respirations would make us think, of course, of a pulmonary involvement of some sort, such as pneumonia, but no evidences of this can be found nor were any pneumococci found in the blood.

Now, in addition to the laboratory work which I have already mentioned, we made a lumbar puncture and obtained a clear, transparent fluid under low pressure, of which we collected 15 c.c. very readily. The Nonne reaction was slightly positive, the Wassermann negative, and there were only one or two cells to the cubic millimeter. Later another puncture was made and the fluid again showed the same characteristics, and the Löffler examination for tubercle bacilli was negative.

The day after admission another blood-count was made, which showed a remarkably high red count, 6,400,000, the leukocytes having diminished to 6500. You will remember that they were 10,000 the day before. Another blood-culture proved sterile, and I may add that several have been subsequently taken and all have remained sterile. *The Widal test was repeated and was strongly positive at the end of forty-five minutes in a dilution of 1 : 40.* No sputum examination was made, for the very simple reason that the patient did not cough or expectorate.

Now when we come to consider the **diagnosis** we find ourselves face to face with a very difficult problem. It is very evident that the conditions in the urine alone do not warrant a

positive diagnosis, nor are they sufficient to make a diagnosis of anything excepting a urethritis connected with his stricture. The real question at issue is: Have we to deal with a case of typhoid? Let us consider the evidence which speaks for typhoid fever. To begin with, the period of incubation is about correct for this disease. We have had a rising temperature, beginning with less than 100° F. and going up to 103° F. within three or four days. Then we have had completely negative findings in all the organs except the urethra. The leukocyte count, to begin with, was 10,000, and is rapidly diminishing, being 6500 the following day. The spleen was not palpable when he came in, nor was I able to palpate it yesterday or the day before. Today I can just barely palpate it. It feels moderately soft, and I think we are justified in concluding that, since we could not feel it when conditions were favorable, the spleen is enlarging. This, of course, speaks for typhoid. The Widal reaction is so strongly positive that we can utilize this as a very strong argument in favor of the case being one of typhoid. The patient states that he has never had typhoid fever and has never been inoculated against the disease. Minor points of evidence are the coated tongue, which is certainly as typical looking as one ever sees in typhoid, and the general stuporous condition. The patient rouses up sufficiently to answer intelligently, but relapses into a semistuporous condition, such as is so often seen in severe typhoid. This about sums up the evidence in favor of typhoid fever.

What have we that speaks against it, or what is it which makes us hesitate to accept this as a frank case of typhoid? To begin with, we have not been able to cultivate the organism from the blood or the urine. We are attempting now to cultivate it from the stools, but the results are not known as yet. This is not very positive evidence against typhoid, since we very frequently are unable to cultivate the organisms from the blood when the patient comes under observation with a well-developed Widal, or, in other words, when the case is well along toward the end of the first week or perhaps in the middle of the second week.

We cannot reconcile the rapid pulse and respirations with the diagnosis of typhoid fever. A slow pulse in typhoid—that is, slow in proportion to the degree of fever—has been recognized for decades as one of the cardinal points in the diagnosis of this disease, and, while we often find it in other conditions, we rarely ever see a typhoid without it. A relatively slow pulse does not speak so strongly in favor of typhoid as does a relatively rapid pulse speak against this diagnosis. If this man had a pulse of 85 or 90, with his temperature of 102.8° F. and respirations of 18, I think we should have made the diagnosis of typhoid without very much hesitancy. As it is now, we have provisionally put the patient upon typhoid orders, but we are leaving the diagnosis open until we can accumulate further evidence.

Differential Diagnosis.—It will be instructive, however, to discuss some of the other possibilities. We might think first of trichinosis, of which I have seen so much in the past year as to make me always suspect it in obscure cases of fever. Against the diagnosis of trichinosis, however, there are many things to be said. In the first place, there is no increase in the leukocytes and there is a progressively developing leukopenia. Second, the differential count shows no eosinophils at all, which speaks very strongly against this diagnosis. Then, the man has had no abdominal symptoms, such as pain or diarrhea, nor has he had any muscular soreness and no tenderness can be elicited over the muscles at the present time. So I think we can rule out trichinosis with some degree of certainty.

Tubercular meningitis must always be thought of. The absence of rigidity of the neck, the normal reflexes, the spinal fluid without any increased pressure, without an increase in the cell count, and the absence of tubercle bacilli in the spinal fluid speak against this diagnosis. These latter considerations also rule out a meningitis of any other type.

The initial chill and the fact that the patient states that he has had repeated sore throats make us think of the possibility of an endocarditis. Against this diagnosis is to be urged the absence of all physical signs in the heart, our lack of success in the cultivation of any organisms in the blood, and the progressive

leukopenia. While it is true that under certain circumstances a patient may be so overwhelmed by a toxemia that he does not develop a leukocytosis in endocarditis, it must also be stated that this is the exception and not the rule.

The one thing that is uppermost in my mind is an *acute miliary tuberculosis of the typhoid type*. There is probably no diagnosis which at times is more difficult to establish, and in some cases almost impossible, than the diagnosis between typhoid fever and this particular type of acute miliary tuberculosis. Let us recall for a moment the conditions under which a miliary tuberculosis develops. Almost invariably there is some, even though a very tiny, old focus of tuberculosis present somewhere in the body. Perhaps there is a very small focus in the lung, too deep to be recognizable clinically. Perhaps a bronchial gland is involved. Occasionally, as in a case I have recently seen, a very small patch of tubercular osteitis is present. Some small focus of this sort, which perhaps has given no symptoms whatever, develops in such a way that it empties its caseous products into the blood-vessels. Several German observers have shown that in a large number of cases of acute miliary tuberculosis the disease can be traced to the development of the tubercle in the wall of a blood-vessel, and this permits of the flooding of the entire circulatory apparatus with tubercle bacilli.

If you will stop to think for a moment of the enormous number of bacilli which are present in even a small amount of caseous material, it will be very apparent to you that under these conditions a single tiny focus can pour a sufficient number of bacilli into the blood to flood the body with miliary tubercles, which develop in innumerable numbers.

Now the characteristic thing about an acute miliary tuberculosis, when the case is typical, is that the tubercles in all the organs are approximately of the same age. I do not mean that there may not be, let us say, a small cavity in the lung or some caseating glands which are not new, but that the great majority of the viscera are simply flooded with tubercles which are very tiny, from a pin point to a pin head in size, and all of

approximately the same age. What I am trying to make clear to your minds is that under these circumstances, even though tubercles may be present in half a dozen of the viscera, literally by millions, yet they cause very few local symptoms. *The liver, kidneys, and spleen may simply swarm with innumerable numbers of these tiny, grayish points without causing any symptoms clinically referable to these organs.* The conspicuous thing about a case of miliary tuberculosis of this type is the complete absence of all physical signs. The lungs are found negative for quite a period of time, and even when symptoms do develop they are very inconspicuous, and consist merely in numerous faint râles scattered throughout the lungs. If these happen to be in the depths of the lung they will not be audible, so that the lungs may be, as I have had opportunity to see at postmortem examinations, pretty well filled with these tiny tubercles and yet no physical signs can be elicited. Of course, in some cases, especially those which run a subacute course, conditions are more favorable for diagnosis, in that a definite bronchitis develops.

Now what is there about a case of acute miliary tuberculosis of such a type which enables us to make the diagnosis, or at least suspect it? My experience is that the things which should put us on our guard are the somewhat rapid respirations and a pretty rapid pulse in a case which looks otherwise like a typhoid. That corresponds precisely with this case. We find everything tallying most beautifully with a typhoid—the period of incubation, the rising temperature, the gradual enlargement of the spleen, the progressive leukopenia, the strongly positive Widal—all of these, I say, point strongly toward a typhoid, but yet there are one or two symptoms which will not fit in, and these are, as I have already said, the rapid pulse and rapid respirations.

If you will notice the patient again I think you will agree with me that he is a little cyanotic, although in a colored man this is difficult to make out. It seems to me, however, that his lips and finger-tips are slightly more bluish than usual.

How about the leukocyte count in miliary tuberculosis?

This varies—different authorities give different answers. My own experience is that there is rarely very much of a leukocytosis in the pure cases, and in many instances there is a distinct leukopenia. It is probably true that the development of the leukocytosis in a tuberculosis depends more or less upon its location. Most authors, I think, state that there is a leukocytosis in tubercular meningitis, although my experience, which is almost entirely, however, with adults and not with children, is that there is usually a leukopenia. Again, many of the discrepancies in this regard are due to the fact that many cases are called miliary tuberculosis which, in my judgment, should not be classified as such.

In the true miliary tuberculosis the tubercles are small, rarely ever larger than a pin head, and pretty regularly distributed all through the different organs. It is not correct to speak of a case as miliary tuberculosis where there is an advanced tuberculosis of the lungs with fairly large foci throughout, and then the development of miliary tubercles here and there in other organs. Certainly this is not clinically or pathologically justifiable. The conception of miliary tuberculosis which we clinicians hold to, is that of an insignificant focus somewhere in the body, generalizing by means of the bloodstream, and generalizing practically simultaneously in all of the organs, so that the clinical picture is that of an acute typhoid-like infection. Occasionally cases will be found where there is a condition of this sort but where the tubercles are abnormally thick in the meninges at the base of the brain, so that the picture is rather that of a tubercular meningitis. In other cases the lungs appear to bear the brunt of the infection, and the symptoms point rather toward an acute infection of the respiratory tract.

To sum up this case, it seems to me perfectly clear that the diagnosis lies between a typhoid and an acute miliary tuberculosis of the true type which I have just described. In view of the strongly positive Widal I should say typhoid, were it not for the rapid pulse, the increased respirations, and possibly the slight degree of cyanosis. You may object, and say that I ought to rule out miliary tuberculosis because I cannot find,

even after the most painstaking examination, any abnormal findings in the lungs. To this I can only answer that in a very rapidly developing case of tuberculosis the tubercles are so small that practically no physical signs can be found for quite a while. We shall, therefore, leave the diagnosis open, and I shall report to you again the further development of the case, or possibly show him to you at our next clinic.

Additional Notes Four Days Later.—I want to report further about the patient I showed you at the last clinic, the young colored man. His condition did not change very materially so far as physical examination was concerned. No rose spots developed and the spleen remained barely palpable. The urine showed no changes. We did not succeed in cultivating the typhoid bacillus either from the blood, the urine, or the stools, nor were we able to cultivate any other organisms from the blood. One thing, however, was decidedly strange. A day or two after I showed him to you the Widal was made again and seemed *very much weaker than it was at first*, when, as you will remember, it was strongly positive. Furthermore, this strongly positive reaction had been checked up by making the test with different strains of organisms, so that there was absolutely no question as to its correctness. When, therefore, it commenced to grow weak, I had the Widal made every day, and the next day it was so weak as to be practically negative. Now it goes without saying that this is exactly contrary to what happens in typhoid fever. If a patient has typhoid fever the Widal in the beginning is absent, then weakly positive, becoming more strongly positive as the days go by. While I am absolutely convinced of the correctness of the Widal in the beginning, I am unable to explain to you why it grew so very much weaker, and, finally, a day or two before death, which occurred on June 17th, it was quite weak.

In one other respect the patient showed a change. On the 12th the leukocytes had gone down to 3700, a very decided leukopenia. On the other hand, the patient's general condition was growing steadily worse. The pulse grew more and more

rapid, ranging from 125 or 130 to an occasional 140, with a temperature range growing steadily lower. The day after I showed him to you the temperature commenced to drop, and in the last couple of days of his life the temperature was not much above normal. Simultaneously, the respirations increased in frequency, so that we had the very unusual picture of a steadily falling temperature with a steadily rising pulse and respirations and a definitely increasing cyanosis.

On the 15th the following note was made in the early morning by my intern: "There is more dyspnea; no signs of lung involvement, no râles, no areas of dulness, no rubs. The respirations are short and rapid, with the inspiratory phase somewhat longer in proportion to expiration than normal." That same afternoon we examined the patient again with great care, and then for the first time we found something abnormal in the lungs. We could hear occasional scattered fine râles, generally in groups here and there. It required the most painstaking examination and very attentive listening to find anything at all abnormal. This was in very striking contrast to the severe dyspnea which had now developed.

As you will remember, we were hovering between the diagnosis of typhoid and acute miliary tuberculosis, and the principal reason why we thought of typhoid was the strongly positive Widal. With the disappearance of this there was no good reason why we should cling to the diagnosis of typhoid, and with the development of these fine, scattered râles throughout the lung, coupled with the rapid respirations and marked dyspnea, we did not hesitate to make the diagnosis of acute miliary tuberculosis of the typhoid type.

The subsequent course was rapidly downward. No further change took place in the physical findings except that the râles became slightly more audible. The patient died on the 17th, nine days after his entrance into the hospital and a little more than three weeks after the initial chill.

Autopsy Findings.—We were fortunate enough to secure an autopsy, which was made shortly after death, and I am sure you will be interested in hearing an abstract of the findings.

In a nut-shell, what was found was a disseminated hematogenous miliary tuberculosis of practically all the organs, but especially the lungs, liver, kidneys, and spleen. There were tiny tuberculous ulcers of the distal ileum barely large enough to be visible, a tuberculosis of the mesenteric lymph-glands, and a small cavity, perhaps the size of the end of one's finger, situated rather deeply in the subapical region of one lung. This had produced no symptoms and no sputum, and we had not been able to elicit it by physical examination. The bladder showed a few petechial hemorrhages in the mucous membrane. The meninges of the brain showed nothing abnormal and no tubercles were visible in them.

This case is, to my mind, one of the most characteristic and perfect examples of a pure miliary tuberculosis which I have ever seen. It is highly probable that the focus which caused all the trouble was the small cavity in the subapical region. This was undoubtedly old, as the walls showed a distinct thickening, and while the point of generalization could not be demonstrated, it is practically certain that this was the source of the organisms which, entering the circulation, led to the flooding of all the organs with tubercle bacilli.

I want to call your very particular attention to two points: In the first place, the tubercles everywhere were of extraordinarily small size, none of them being larger than a small pin head. The second point is that the lungs were so thickly sown with them that one could hardly find a point of normal tissue macroscopically. This is particularly interesting when one stops to think that in spite of our close watch upon the physical findings in the lung, *it was not until a few days before death that even a single râle was audible.* It is difficult to understand why this should be so, unless it be that the majority were deeply situated and they could not be heard. Be the explanation what it may, I can vouch for the fact that with both of my interns and myself constantly on the watch for pulmonary findings, none could be detected until this time, and then they were only to be heard with difficulty and on most attentive listening, in the form of very tiny dry and moist râles. I regret that the patient could

not have lived long enough to have been shown in the clinic again today, although there was objectively not very much change.

This case illustrates better than reams of paper might do the great difficulties which lie in the differential diagnosis between typhoid and acute miliary tuberculosis. Had this patient not had the rapid pulse and increased frequency of respiration we should, in all probability, have contented ourselves with doing the Widal reaction only once or twice and calling the case one of typhoid fever. Fortunately, the repetition of the test a number of times showed that it was growing progressively weaker, and removed the one difficulty which stood in the way of the diagnosis of acute miliary tuberculosis.

To sum up the whole case, we had a man in early middle life entering the hospital with the history of two weeks of fever initiated by a chill. The temperature rose gradually for four or five days with a relatively rapid pulse and rapid respirations, but no physical findings worth mentioning. The leukocyte count of 10,000 on admission dropped to 6500 and later to 3700; blood-cultures, urine-cultures, stool-cultures, and spinal fluid findings were all negative. The further course of the disease showed a dropping temperature, the pulse and respirations remaining high. The diagnosis was only made possible by the development of these fine râles in the lungs where none had been heard before, taken in conjunction with the rapid pulse, respirations, and the cyanosis.

I do not believe that I mentioned that the eye-grounds were examined repeatedly for miliary tubercles, but we were not able to find any at any time.

There is one point still to be explained. What was the cause of the patient's blood showing the strongly positive Widal reaction? The autopsy did not disclose anything which in any way cleared this up. There were no lesions in the intestine pointing toward an old typhoid, and cultures made from the gall-bladder did not reveal any typhoid bacilli. I requested that this be done, thinking that the patient might have been a typhoid carrier. I am perfectly certain of the correctness of the findings,

since the test was repeated with various strains of organisms, so we shall simply have to note the fact that the patient showed a positive Widal which subsequently became negative. Once before, while a student in Vienna, I saw a similar case in which one of the world's best diagnosticians had made a diagnosis of typhoid under almost the same conditions that had existed in this patient, noting, however, that the respirations and pulse seemed more rapid than ordinarily. A week or ten days later the diagnosis was cleared up in that case by the development of miliary tubercles in large numbers in the choroid. In this case the Widal showed a strongly positive reaction in a very high dilution, and this was also checked up by making the test with different strains. The autopsy revealed precisely what was shown in this case—namely, a pure miliary tuberculosis with no evidence of a previous typhoid infection. I do not remember whether in that case the Widal became weaker before death or not.

One final point in this case is worthy of note. While a positive Widal reaction is a strongly probable criterion of typhoid, it is by no means absolutely certain, and in each and every case one should not be satisfied with a diagnosis of typhoid until the organism itself has been cultivated.

A CASE OF SYPHILIS OF THE LIVER

Discussion of the Various Pathologic Forms of Syphilis of the Liver. Clinical Grouping of Cases Under (*a*) Cases Resembling Cirrhosis; (*b*) Cases Resembling Malignant Tumors; (*c*) Febrile Cases Resembling Abscess of the Liver. In Doubtful Cases the Serologic and Therapeutic Tests Should be Used to Clear Up the Diagnosis.

THIS patient is sixty years of age, a native of America, and comes into the hospital with the following complaints: First, pain in the upper part of the abdomen; second, slight swelling of the legs and abdomen; third, cough; fourth, shortness of breath. He says that his trouble began approximately three years ago, and that he has been subject to these symptoms in attacks since that time. The attacks have become more and more frequent and the present one started a few weeks ago. During this last attack his legs and abdomen began to swell and he developed shortness of breath and pain in the abdomen.

The patient states that the swelling of the legs started before the enlargement of the abdomen, although he is not very sure about this. The shortness of breath existed even between the attacks and has been practically continuous for the past two or three years. The pain is situated in the epigastrium, is dull, does not seem to be definitely related to meals, although in a general way it comes on with a full stomach, but it is not relieved by the taking of soda or other drugs. There is no vomiting. The pain has also been present almost continuously for two or three years.

The cough has been unproductive as a rule, only occasionally has there been any sputum, and never any blood.

He has noticed for a long time that he urinates more frequently, especially at night, sometimes having to rise eight or ten times during the night. He thinks he does not urinate a large amount and has never passed any blood.

Habits.—The patient has used tobacco all his life; he drinks beer and whisky occasionally. The bowels are generally constipated. His sleep is disturbed by the frequent urination.

Family history is negative. He has been married for thirty-five years, has a son thirty-three years old, and his wife had two miscarriages, both of which occurred before the birth of the boy.

Physical examination shows a rather poorly nourished man of about sixty, with the skin definitely subicteric. The icterus is especially well seen in the conjunctiva.

Head and Neck.—The eyes react to both light and accommodation. The teeth are carious, and one shows an abscess cavity about the gum. The neck is negative.

The *chest* is poorly developed; expansion is fair.

The *lungs* are negative.

The Heart.—The apex-beat is in the fifth intercostal space, approximately in the nipple line. The left border is about 1 inch further out than normal. The right border is also further out than normal, and this enlargement is principally in the transverse direction. The tones are clear, but the heart beat is irregular and there are many extrasystoles. This is easily checked up by the pulse tracing.

The *abdomen* is distended, but fairly soft. On admission there was dulness in the flanks and over the pubes which shifted very readily, and the fluctuation wave was readily elicited, so that there was no question that a considerable amount of fluid was present in the abdominal cavity. This is now rapidly disappearing.

The liver can be readily felt $1\frac{1}{2}$ inches below the edge of the ribs. The edge is rounded and can be followed out fairly continuously. One can feel a deep incisure in the edge of the liver which is sufficiently large to permit the placing of the edge of the hand in it. What is apparently a second notch can be felt further to the left.

There is an old scar over the gall-bladder region. The patient states that he was operated fifteen years ago for what was apparently some gall-bladder trouble. We learn that he had typhoid fever just before this operation, so it is quite likely, in

view of the fact that his sickness came on suddenly, that it was a cholecystitis following typhoid. He says he was told that they drained pus from him at that time.

The spleen could not be palpated when he first came into the hospital, but is now readily palpable 1½ inches below the costal margin.

If we go back now to examine the liver a little more carefully we shall find what is apparently a tumor mass in the epigastrium. We have followed this mass very carefully for many days, and our conclusion is that it is not a tumor, but a portion of the liver approximately the size of one's fist which stands out very prominently in the epigastrium, and is made particularly conspicuous because of the deep notches already referred to.

The further examination of the patient discloses little of importance. The genitalia are somewhat edematous, the left testicle and epididymis rather larger and harder than normal. The lower extremities show only a very slight degree of edema together with slightly varicose veins. The reflexes are all present and normal.

The *urine* shows a specific gravity of 1020, acid reaction, contains a moderate amount of albumin, and has averaged about 1500 c.c. daily. As his condition has improved somewhat, the amount of urine has decreased rather than increased.

The *blood-pressure* on entering the hospital was 235 systolic and 134 diastolic, but has come down a little bit, so that it now averages about 200 systolic and 120 diastolic. A blood-count showed hemoglobin of 80 per cent. and a white count of 12,500. The differential count showed 80 per cent. polymorphonuclear neutrophils, 11 per cent. small mononuclears, 3 per cent. large mononuclears, 1 per cent. eosinophils, and 1 per cent. transitionals.

Repeated stool examinations have given negative results, particularly as to occult blood.

Now, if we analyze this case somewhat we shall see that it is quite clear in some respects and rather obscure in others. Beginning with the condition which seems most definite, we can be sure that the patient has a chronic nephritis, or at least a high-

grade sclerosis of the abdominal blood-vessels. This is made practically certain by the very high blood-pressure, with persistent albuminuria and a twenty-four-hour amount as high as 1500 c.c. in spite of the fact that the patient has been on a low diet and has been purged considerably. That this blood-pressure has existed for a long time is shown by the heart, which is not only dilated, but markedly hypertrophied, the apex-beat being strong and heaving.

It is not this kidney condition, however, for which I wished to show you the patient, but something very different. The shortness of breath and the slight edema of the feet might very well be explained by a secondary dilatation of the heart as a result of the high blood-pressure. The presence of a considerable amount of fluid in the abdominal cavity was decidedly out of proportion to the slight degree of edema of the feet which he had when he came in. In other words, while the patient thinks he noticed the swelling of the feet first, it seems to me perfectly clear that the edema of the feet did not precede the ascites, but *vice versa*, because we found a very respectable amount of fluid in the abdominal cavity, whereas the edema of the ankles was rather trifling.

Then we did not find the very marked tenderness over the liver which we are accustomed to find in cases where the swelling is due to venous congestion alone. Furthermore, a liver which is enlarged to this degree as the result of stasis would show a fairly uniform, sharp edge with no notches or projections on the surface. There would also be no such enlargement of the spleen as we find in this case. So, leaving the high blood-pressure, the heart and the kidney condition out of consideration, let us ask ourselves what the condition in the liver is, because that is the real problem before us.

Briefly, the findings in the liver can be summed up as follows: The liver extends about $1\frac{1}{2}$ inches below the costal margin, is hard, with a rather indefinite rounded edge showing two very large notches. Between these incisures is a tumor or, as we believe, merely a large protuberant portion of the liver. These findings in the liver, with the subicteric tint to the skin and

conjunctiva, a moderate enlargement of the spleen, and a moderate ascites constitute the essential pathologic picture.

Does it seem possible that this condition dates back to his operation fifteen years ago? This seems extremely improbable, since the patient describes his sickness at that time as coming on with an acute fever and tenderness in that region, and says he was told by one of the best of our surgeons that he had pus there and must be operated at once. In view of the fact that this followed shortly after a severe typhoid, which is notoriously prone to produce cholecystitis, and in view of the further fact that the incision was made over the gall-bladder, it seems highly probable that what he had was a cholecystitis. He recovered from this completely, he says, the drainage-tube was removed in a few weeks, and he felt perfectly well until the present disease started two or three years ago. He has noticed that the upper abdomen was becoming more prominent recently, but paid no particular attention to it. He is quite sure that this tumor-like projection has been there for a couple of years only.

Aside from the symptoms we have already referred to, the shortness of breath, frequent urination, etc., he complains of very little except dyspepsia. On the whole, he has felt himself to be in pretty good condition and is more disturbed now over the ascites than over anything else. He has had no very serious loss of weight, no vomiting, and no blood in the stools. Nothing points toward any malignant condition in the gastro-intestinal tract, although our first thought was that this condition was probably a secondary carcinoma in the liver following a carcinoma of the stomach or some other of the viscera. We have had the patient under observation now for approximately a month, and not only has his condition not become worse, but he has improved to a very remarkable degree. His ascites is going down steadily, the edema in the legs has disappeared almost to the vanishing point, the tenderness over the liver is less than it was, and while his blood-pressure is still very high, as might be expected, it is somewhat lower than it was in the beginning. We feel that we can eliminate carcinoma in this case because of the long duration and the rapid improvement under treatment.

The second thing which occurred to us as most probable was that he had some type of cirrhosis of the liver. The physical findings in this case are peculiar, in that the liver is not only large and hard, but has a big protuberance and two large, deep incisures in it. This is the condition which is typical of one of the forms of syphilitic cirrhosis, the so-called botryoid liver. While the patient has given no history of syphilis, we know that his wife had two miscarriages immediately after their marriage. A Wassermann test was accordingly done on both blood and spinal fluid. The blood was negative, but the spinal fluid was strongly positive, so we have some confirmation that the condition is syphilitic. The patient was put upon a vigorous antiluetic treatment in the form of daily inunctions of mercurial ointment with rapidly increasing doses of potassium iodid, and to our satisfaction we found that the condition began to improve very promptly. The tenderness over the liver is distinctly less than it was. The liver does not seem to be any smaller than it was before, but, as we shall see in a moment, this was hardly to be expected. The ascites, however, is clearing up rapidly, which would hardly be the case in an ordinary alcoholic cirrhosis.

Pathology of Syphilis of the Liver.—What I want particularly to discuss on the basis of this case is the manner in which syphilis attacks the liver, because of all the forms of visceral syphilis—leaving out of consideration syphilis of the brain and cord—syphilis of the liver is one of the most frequent and important, and at the same time one of the most obscure and difficult to recognize. Syphilis of the liver may be either congenital or acquired. The congenital type consists generally of a diffuse sclerotic process with or without actual gummata, and this occurs nearly always in early life.

In acquired syphilis we find changes in the liver occurring both early and late. During the secondary stage of syphilis we occasionally find jaundice together with a slight swelling and tenderness over the liver. The interpretation of this is not perfectly clear. Some men have considered it to be an ordinary catarrhal jaundice which happened to attack a syphilitic patient. Possibly the gastro-intestinal disorders which are frequently induced

by treatment may help to produce this gastroduodenal catarrh. On the other hand, many of our best clinicians believe that what actually occurs in these patients is an acute inflammatory change in the bile-duct due to syphilitic infection, and they adduce in support of this view the fact that it clears up under antiluetic treatment. In my opinion, this is not a common condition, and is certainly vastly less important than the changes in the liver produced late in the disease, during the so-called tertiary stage. The internist sees practically all of his cases during this stage; at least that has been my experience.

In the liver, as elsewhere, the typical lesion is the gumma, an opaque, firm, solid mass, caseous in appearance, but much firmer than the caseous material in tuberculosis, surrounded by a whitish ring of young scar-tissue, and this again by a translucent zone of small-celled infiltration. These gummata may be very large. I do not think it is generally appreciated how large gummata of the liver may become. I have seen them the size of one's fist, and only recently we had a case where a gumma in the spleen had attained the size of a grapefruit. These gummata may occur singly or, what is much more common, in large numbers, and they nearly always can be felt on the surface when they are multiple. As a result of these multiple gummata the liver is greatly enlarged. When they begin to heal, either spontaneously —because they do heal spontaneously under certain conditions —or as the result of treatment, they are replaced by bands of connective tissue which cut deeply into the organ, producing great furrows. If the gumma is a small one, the furrow may be only a fraction of an inch in depth, but if the gumma is a large one, or if there are several together, incisures a couple of inches in depth are produced. In very marked cases a condition resembling multiple lobes in the liver results, which has given rise to the term *hepar multilobatum;* that is, the multilobulated liver which is so very characteristic of the late tertiary stage of syphilis of the liver. One may have every transition between multiple gummata and this lobulated condition, or they may coexist. One may find gummata in a lobulated liver. It is principally a question of the age and course of the disease. The lobulation is due

to the scar tissue which, of course, takes the place of the disappearing gumma.

Fig. 44.—Syphilitic liver. Hepar multilobatum. (Courtesy of Dr. Burmeister).

Substantially, then, we can say that the great majority of cases of syphilis of the liver in adults which come under the observation of the internist occur late in the disease. The anatomic changes, broadly speaking, consist of gummata with or without

diffuse changes, and the sequelæ of gummata—namely, scar tissue —producing in the most characteristic cases the lobulated liver. It is, of course, not my purpose in a clinical lecture to go into the pathologic anatomy of this subject, but it might be well to impress upon you that in some cases gummata of the liver look extraordinarily like carcinomata even on the postmortem table, so it is not to be wondered at if a mistake is occasionally made clinically.

Symptomatology.—The clinical history of these different types varies very greatly. It is interesting to look over the chapters on this subject in the various standard works and see how differently the clinical picture is portrayed. This is easily understood when we reflect that the gummata may vary in number and size to an extraordinary degree, and that many of the clinical symptoms produced by them are, as it were, accidents of location due to pressure upon some particular structure, such as the bile-ducts or the portal vein. As regards frequency, my experience leads me to say that, regarded as a clinical entity, syphilis of the liver is by no means as rare as it is portrayed by some authors. Certainly in a large hospital, such as the Cook County, one sees a very considerable number of cases. Second, while the clinical history varies very decidedly in different cases, they may all be grouped with a fair degree of accuracy under three heads: (*a*) Cases resembling cirrhosis; (*b*) cases resembling malignant tumors; (*c*) febrile cases resembling abscess of the liver. Some authors, notably Rolleston, make a more extensive classification, but it seems to me that the grouping just mentioned, which is in wide use, is the most satisfactory.

In the first group the case develops almost precisely as a case of ordinary Laennec's cirrhosis. In many instances one has not the least suspicion that it is in any way different from this type, and it is only when the evidences of syphilis are discovered elsewhere in the body, or when the Wassermann reaction is positive, that the real etiology is made manifest. In a general way one can say that ascites is not so likely to develop and recur, and that jaundice is much less apt to be high grade even in the late stages of a syphilitic cirrhosis than in the alcoholic cirrhosis.

In many instances it is the shape of the liver itself which gives the clue to the diagnosis. If the liver is sufficiently large to be readily palpable, as it often is, and one can feel large notches, such as you see in the illustration, which is a reconstruction of a case of this sort, then the diagnosis is fairly simple, for under no circumstances does an alcoholic cirrhosis ever show incisures of anything like this depth. The lobulations or, more properly speaking, granulations in Laennec's cirrhosis are small, varying from the size of a pin head to two or three times that size. The liver is hob-nailed but not lobulated in the proper sense of the word.

The diagnosis of a case of this kind is practically impossible to make with certainty unless the typical indentations on the surface of the liver can be felt. The spleen offers no differential point, since it is frequently enlarged. Indeed, in some notable instances of syphilis of the liver the spleen is as large as in cases of splenic anemia. Occasionally one sees a case of syphilitic cirrhosis resembling the hypertrophic cirrhosis of Hanot; that is, showing a large spleen, fever, and considerable jaundice. In my experience this is exceedingly rare, although I have seen one or two well-marked instances. More than once I have made the diagnosis of an alcoholic cirrhosis where the patient was a drinker, but because of a positive Wassermann reaction have put the patient upon antisyphilitic treatment, and, to my surprise, have seen the condition rapidly clear up, thus making the diagnosis *ex juvantibus*. It need hardly be said that this is scarcely a scientific method of making the diagnosis, yet such are the limitations of our knowledge that we are occasionally compelled to resort to it.

Only such cases are susceptible of great improvement in which actual gummata are still existing. If these have been entirely replaced by cicatricial tissue, as in a typical lobulated liver, it is very unlikely that any great improvement will result from the administration of mercury and iodids. Probably a great many of the supposedly alcoholic cirrhoses which have been cured are, in reality, cases of syphilis of the liver.

Under the second group of cases we find that tumors of the liver may be imitated to a nicety by syphilis. The patient comes

under observation with a big liver, and one can feel tumor masses varying in size from a hickory nut to an apple. Generally there is a good deal of pain due to the perihepatitis, which is considered by some authors as highly characteristic. Often there are digestive disturbances, and the whole picture impresses one as being that of a malignant neoplasm of the liver. Within the past year I have seen such a case where for the first week that the patient was under observation I had little doubt that the case was one of metastatic carcinoma. A strongly positive Wassermann reaction, together with some suspicious cutaneous symptoms, led me to suggest the use of iodid and mercury, and the rapidity with which the nodules disappeared left no room for skepticism as to the diagnosis. Such cases have been abundantly recorded.

Two symptoms are so common in diseases of the liver that they require special consideration—namely, ascites and jaundice. From what I have said in regard to the pathologic anatomy it must be sufficiently obvious that the development of these will depend very largely upon the location of the gummata and the resulting connective tissue. If a number of gummata should be so close together as to impinge upon the portal vein, ascites will result. If they should be so numerous as to obliterate many branches of the hepatic duct, jaundice would be likely to result, so that one cannot make any statement in regard to these two symptoms which will hold in every case. As a matter of fact, jaundice is considerably rarer than ascites.

In the third group of cases another symptom predominates—namely, fever. Numerous authors, and quite recently Pel, have emphasized this symptom. It must not be thought that this fever is a rare symptom, because it is not; it is quite common, and particularly so, perhaps exclusively so, when gummata are present and growing rapidly. In any event, the cases which I have observed where fever was most marked were nearly all cases where there was good reason to believe that there were numerous gummata present. I am not at all clear in my own mind that the fever is actually due to the syphilitic process, because, as is well known, malignant tumors of the liver may produce an identical fever. I have seen carcinoma of the liver running a course which

looked like typhoid fever. It is highly important that one should remember that even with a moderate enlargement of the liver the fever in these syphilitic cases may be quite considerable and often of the recurrent type. There is the greatest possible danger of assuming the existence of an hepatic abscess, and perhaps subjecting the patient to an unwarranted operation, particularly if the patient has been in some locality where amebic dysentery occurs frequently.

This sketch of the diverse clinical symptoms which may exist in syphilis of the liver will, I trust, make it sufficiently clear to you that it is very important in any unusual condition of the liver to think of syphilis. The Wassermann reaction, both on the blood and spinal fluid is, of course, a great help, and in any doubtful case the effects of treatment should be tried, and this will occasionally clear up a very obscure condition.

The **prognosis** of these cases depends almost entirely upon the number of gummata and the amount of liver tissue destroyed. If the case is seen while gummata are still active, they respond to treatment in a most remarkable way. Occasionally one will observe a big, nodulated liver shrink in size and the nodules disappear in the course of a few weeks' treatment in a most astounding way. On the other hand, if the liver is one in which there is nothing but scar tissue, or in which this predominates, very great improvement can scarcely be hoped for.

I surmise that in the case before you both conditions coexist. There is undoubtedly a large amount of connective tissue and probably some gummata are still present. Otherwise the improvement would be difficult to explain. This case is by no means as clear a one as many others I have seen, since it is complicated by the kidney condition.

Treatment.—It is hardly necessary to say much on the subject of treatment. This patient has been receiving mercurial inunctions daily, and we have been pushing the iodids pretty vigorously. My experience with salvarsan and neosalvarsan in such cases has been very limited, but the results did not differ materially from those obtained with the older remedies. It would certainly be unwise to rely upon them to the exclusion of mercury and the iodids.

CLINIC OF DR. ISAAC A. ABT

MICHAEL REESE HOSPITAL (SARAH MORRIS MEMORIAL HOSPITAL FOR CHILDREN)

FEEDING THE NORMAL BABY WITH ARTIFICIAL FOODS. FOOD PREPARATIONS

General Principles of Infant Feeding with Cows' Milk. Caloric Versus the Percentage Method. Necessity for Scientific Study of Digestion and Metabolism in Infants. Use of "Certified Milk." Prevention of Milk-born Epidemics. Quantity of Food at Each Feeding. Frequency of Feeding. Energy Value of Infant's Food. Chemistry and Preparation.

Feeding Normal Babies with Artificial Food.—This morning I want to talk about some of the general problems of feeding infants. Let us consider the subject of feeding normal babies; that is, feeding normal babies with artificial food. If one were to take a census among recent graduates in medicine concerning the greatest bug-bear in medical teaching, it would be voted almost unanimously that the subject of infant feeding is the most difficult to grasp and is presented in the most intangible manner of any subject in the curriculum. It was formerly said that no obstetrician had arrived at distinction until he had modified an obstetric forceps and labeled it with his name. And so it may be said of teachers in pediatrics: no pediatrician is truly great until he has evolved some new method of infant feeding and attached his name thereto.

Every conceivable plan has been invoked for modifying or adapting cows' milk for artificial feeding. It would be an absurdity to enumerate them.

Those men who have been devotees to one single method, in some instances have become enslaved themselves, and have

exacted the strictest allegiance from their followers. Any deviation from one of these sanctified methods was viewed as a sacrilege.

Those of us who have lived long enough to accumulate an experience of our own must have learned that no one method is applicable to every case. We have learned very often from our bitter experience that the method which was crowned with the greatest success in one case met dismal failure in another. Our own statistic summary of results did not correspond with those which appeared in current literature or in the proprietary infant-food propaganda. Our babies have not always looked like the ruddy faced infant who appeared on the label after taking two cans of the "Never Fail" infant's food.

The subject of infant feeding has usually been taught as this or that man's method by figures on the blackboard involving algebraic calculations, whereas it should be taught at the bedside and in the laboratory. It is my own idea that the subject should be taught candidly, not dogmatically. Physicians should know from the outset the limitations of artificial feeding, the high mortality attendant upon its use, and the general principle that no plan of artificial feeding or food is applicable in every case.

Students should have it impressed upon them time and time again that *the only specific food for an infant is mother's breast milk*, and every energy should be bent to conserve the specific food for the infant.

We should endeavor to be resourceful, not to try one food after another in a haphazard manner until the gamut has been run, to say nothing of exhausting the baby's digestive and assimilative powers. We should be taught the general principles of food and feeding.

A vast amount of work has been done in the past ten years by scientific workers in pediatrics on the physiology and pathology of infant digestion and the chemistry of infant food.

Perhaps it is not going too far to say that in no department of human knowledge has the pendulum swung so far as in the subject of infant feeding. One school has taught that the preservation of life, the prevention of rickets, and the treatment of con-

stipation depended upon a high fat content. At this moment another school teaches that the preservation of life, the prevention of disease, and the cure of constipation depends upon low fat diet.

The general principles of infant feeding should involve a most searching study of the physiology of nutrition. The chemistry and digestion of fats, proteins, carbohydrates, and salts, their assimilation in the body and disposal through the excrement, should be investigated in the most thorough manner. The study of nutrition in the infant consists not only in an understanding of his digestion, but equally as important is an inquiry into the functions of metabolism.

We have recently learned that the alimentary intoxications depend not only on perversions of digestion, on fermentation, and decomposition in the gastro-intestinal tract, but, what is equally important, on the constitutional effects resulting from the perversion of the processes of *intermediary metabolism*. The hypothesis that the molecule of fat or the molecule of protein, elaborated from a non-specific milk, may not combine with the cells in the intermediary metabolism is not only of scientific but also of practical interest. This hypothesis offers an explanation why the up-building processes of the body do not go forward, why the infant loses or remains stationary in weight despite the fact that he is receiving an abundance of food.

Great stress should be laid upon the abnormal states which result from an excessive amount of any component element of the food. Just the same emphasis should be laid upon abnormal states resulting from a deprivation of food elements. While it is of great importance to impress the lessons of digestion and metabolism, it is equally important to lay great stress upon the energy value of foods. Thus, the following problem presents itself: The baby is digesting well, but is not gaining in weight. What change may be made in the infant's diet which will increase the energy value of the food without impairing digestion? It is important to consider the necessary facts concerning the frequency and quantity of feedings and the dangers of overfeeding as well as underfeeding. In order to complete our understanding

of the food mixture we should inquire into the percentage composition of food, particularly milk, and we should attempt to interpret the percentage value of food mixtures. Thus we will know at a glance whether the baby is receiving too much fat or too little, or too much protein or too little. To compute all in caloric values and to forget chemical composition is to ignore accumulated data of inestimable value, and to narrow the horizon, to limit the resourcefulness, and to enslave practitioner and student alike to a single method.

It should be our constant aim to correlate the more elementary aspects of food physiology, percentage, and energy value with the clinical aspects of a given case. Not only should we know the proper feeding in disease, but, what is perhaps more important, how to feed so as to prevent disease, and we should learn how to interpret symptoms resulting from improper feeding which threaten to produce illness or, as Finkelstein describes the severe types, "catastrophies." Danger signals, such as tympany, vomiting, rapid breathing, soporose states, or unconsciousness, indicate that feeding should be temporarily stopped. Aside from the increase in body weight there is no better index of the function of digestion and assimilation than the examination of the stool. The student should be taught to examine this in health and disease, both macroscopically and microscopically, and it should be interpreted in its relations to the digestive and metabolic functions of the infant.

In the same way the relations of the urine to feeding and perversions of feeding have a very distinct meaning; excessive excretion of ammonia in the urine means acidosis, the presence of indican means intestinal putrefaction, and glycosuria may under some circumstances indicate alimentary intoxication.

Thus, to sum it all up, infant feeding should not consist in using one man's method. The really great physician retains a historic consciousness. He delves into the past while he utilizes the information which is accumulating from contemporaneous investigation. The teaching of science is not like the production of the modern newspaper, which would discard as unreadable all items which are more than twenty-four hours old. All the well-proved

theories should be imparted to the student. All well-grounded principles should be laid before him. We should not attempt to lay down the subject of infant feeding as a problem in mathematics, which can be proved by an absolute method. We should combine the clinic with the more theoretic considerations. We should make the teaching extensive, giving it a wide range; not intensive. We should endeavor to increase the resourcefulness of the student by teaching him all the methods and the scientific processes which underlie their evolution.

The great importance of putting every baby on breast milk has been emphasized, giving every baby its natural food, but there are times, of course, when this is quite impossible. Now, when we are compelled to feed the baby in some other way than by natural food we select cows' milk as a rule. Cows' milk is an article of commerce and is to be readily obtained. The objections to cows' milk are based upon the chemical composition, the biologic conditions of the milk, and the hygienic conditions under which it is obtained, but, nevertheless, cows' milk is the form of food that is commonly employed. Just a word with regard to the kind of cows' milk that is to be used: The ordinary dairy is not clean, no particular care is taken as to the hygiene of the barn or the surroundings; no particular care is taken as to the hygiene of the milk or the utensils in which the milk is obtained, and consequently the ordinary commercial milk is very likely to teem with micro-organisms of various kinds, and. in addition, may contain pathogenic organisms and be a carrier of disease. Milk may undergo chemical changes; it may sour or undergo putrefactive changes. Attempts have been made to provide satisfactory milk for infants that does away with a good many of these objections. In this country, under the leadership of Henry L. Coit, of Newark, New Jersey, "certified milk" had its inception. This "certified milk," as everybody knows, is a milk which complies with the highest standard of purity. First of all, it is obtained from cows that are supposed to be free from tuberculosis and other diseases. Then, in addition to this, the "certified milk" is obtained from dairies where the highest hygienic methods

are employed; that is, the buildings are clean, no other animals (dogs, cats, or even horses) are allowed in the barn or in the barnyards. The stables are provided with free and ample air supply. Special forms of ventilation are recommended for these dairy barns. The stalls must be open and the animals must be comfortable in them. The droppings from the animals are allowed to fall into a gutter that can be readily flushed. Thus the offal can be removed very soon from the animal house. The animals are not allowed to lie in their own excrement; the bedding is frequently changed and the feeding is carefully supervised.

These animals in the summer-time are allowed to run in the pastures; they are also fed grain, hay, etc., and in the winter-time are fed ensilage. Ensilage is the fodder cut up and stored when fresh and green in large vats or silos, and there preserved. In addition to this, the animals are given pure water to drink. They never are allowed to drink from stagnant pools or from infected wells. These hygienic precautions are taken in order to produce "certified milk."

Then, in addition to this, the milkers are required to take every possible precaution to prevent propagation of disease. If they themselves are sick with colds or with any infectious disease, or with tuberculosis, they are not permitted in the barns. Or if the milkers have contagious disease in their homes they are not allowed in the barn. For instance, it has not been an uncommon experience that an epidemic was conveyed through great areas because some milker was a disease carrier. We know of epidemics that occurred in the northern part of this city where it was pretty well shown that scarlet fever was distributed by the milk. The epidemic originated from a case of scarlet fever in one of the milker's family, the infected milk brought the infection to the consumers' homes, and *the disease* received wide distribution. This must be avoided.

Then, in addition to this, the milker must be clean. In the real "certified milk" dairies the milker scrubs his hands when going from one animal to another. He must be clean in every respect. The utensils are of great importance. For instance,

the pails into which the milk is received are absolutely sterile, and then the milk is transported as soon as possible to the cooling house, where it is cooled at the earliest possible moment. You know if milk is allowed to stand in a warm place micro-organisms multiply to a surprising degree. If milk is cooled rapidly bacterial growth is inhibited. The milk from the cooling-house is bottled under rigid aseptic precautions and the bottles are sealed and put on ice. This care is given to milk all along the line. In its transportation to the city it is not allowed to remain for days in the hot freight cars standing in the yards, nor is it allowed after its delivery from the milk depot to stand on the porch of the consumer on a hot summer's day subjected to the hot broiling sun. Any error in the technic may spoil the quality or the purity of the milk.

Such is certified milk. All milk for baby food should be produced as has been described.

Chemistry of "Certified Milk."—The ordinary "certified milk" is supposed to contain 4 per cent. of fat, 4 per cent. of sugar, and $3\frac{1}{2}$ to 4 per cent. of protein. You know that the milk of animals varies much as to the amount of fat. For instance, a Jersey cow, or a Guernsey cow, or sometimes one of the large brown Swiss cows will contain $5\frac{1}{2}$ per cent. of fat, whereas some of the other animals, like the Holstein or American red cow, average about $3\frac{1}{2}$ to 4 per cent. of fat. In the "certified" dairies, in a good many of them at least, it is the custom to mix Jersey and Holstein milk, one milk containing about 5 per cent. and the other about 3 or $3\frac{1}{2}$ per cent. of fat, and the mixture gives an average of 4 per cent. In this way the average, or the 4 per cent. fat milk, is fairly well maintained.

As a rule "certified milk" is only obtainable in the large cities. Where the hoof-and-mouth disease has been rampant throughout the breadth of the land, it has been considered necessary to pasteurize "certified milk," so that even "certified milk" is not always above suspicion.

In those cases where "certified milk" cannot be obtained, where there is a suspicion that the milk may be infected, it may be scalded; that is, brought to the boiling-point and held there

two or three minutes, or it may be pasteurized by being held at a temperature of 160° to 170° F. for twenty minutes.

Milk-borne Diseases.—We know very well that typhoid fever is frequently conveyed by milk, and some of the lesser epidemics that we have to do with in cities are due to an infected milk-supply that originates most likely on the farm.

As far as tuberculosis is concerned, there has been a great deal of discussion whether it is commonly conveyed by milk. There can be no doubt that milk is susceptible to infection with tuberculosis and that it is a favorable host to the tubercle bacilli. Indeed, in some countries where bovine tuberculosis prevails, among infants and even among adults, milk is a prolific source in distributing this form of tuberculosis.

Now another point is that in some countries milk is derived from other animals than cows. For instance, among the Italians and those living in the islands south of Italy in the Mediterranean milk of goats is very commonly employed. This is also true of the Central American States and South American States. I suppose most of you have seen the photographs of the baby that is applied directly to the mamma of the goat. The Cuban traveler sends these postals to his American friends. The goats' milk is in some ways very good, because it is supposed to be free from tuberculosis. This is not absolutely true, however. If the goats were crowded in barns and dairy yards as cows are at the present time possibly there would be more tuberculosis among them. There is no objection to goats' milk; the fat is rather high. You will find it is impossible to separate the fat from the rest of the mixture unless the milk is boiled first. We have used goats' milk in this hospital. There was a time when we had a large herd in the hospital yard, and milked them each morning and evening and supplied the babies with this milk. Our results were the same as with cows' milk—some babies prospered and others did not.

Quantity of Food at a Feeding.—The widest difference of opinion seems to prevail as to the quantity of food to be given at each feeding. There has been no definite scientific basis up to some time ago even in breast feeding. The breast-fed baby was al-

lowed to continue nursing until he regurgitated or vomited. If the baby fell asleep after nursing he was thought to have had sufficient food. If he remained awake or cried he was thought to be underfed. The amount of food required by the baby at an individual feeding depends upon the degree of dilution of the milk or the frequency of feeding. For example, a baby receiving only five feedings in a day will require a larger volume of food at an individual feeding than a baby that is receiving eight or ten feedings in a day. Or, assuming that a baby is receiving whole undiluted milk, he would require a smaller volume of food than a baby that receives diluted milk. The quantity of food at a feeding is very often an individual problem. The old observations on the capacity of the baby's stomach are no longer relied upon. The measurements were made upon the stomachs of dead babies, but we know that shortly after milk is swallowed some of it begins to pass through the pylorus into the intestines, and thus to speak of a constant capacity of the infant's stomach is not correct. Experience teaches, however, that the average newborn baby on the third or fourth day takes 1 to 1½ ounces at a feeding; at four weeks he takes 2½ or 3 ounces at a feeding; at three months, 3½ to 4 ounces; at four months, 4½ to 5 ounces; at five months, 5 to 6 ounces; at six months, 6 to 7 ounces; at eight months, 8 ounces, and from this time to a year 8 ounces of food is usually sufficient at a feeding.

It must again be emphasized that these figures vary within certain limits, and individual experience with the baby must decide the quantity of food which he can comfortably take.

Frequency of Feeding.—There is also a wide difference of opinion as to the intervals which should elapse between the feedings; that is, the number of feedings in twenty-four hours. In many parts of the United States, England, France, and Italy babies are fed from eight to ten times in the twenty-four hours. This applies to young infants. The number of feedings is gradually diminished with increasing age. In Germany babies are fed five to six times in twenty-four hours and the four-hour interval has received wide adoption. After all, the frequency of feeding is very largely individual with the baby and with the physicians.

According to Czerny's teaching, it requires two to three hours to digest breast milk, and it requires three to four hours to digest cows' milk. Consequently, according to this school, artificially fed babies receive four feedings in the day and one at night. Czerny calls attention to the fact that a newborn baby during the first days of life awakens only three or four times a day for food if he is undisturbed. He also emphasizes the fact that overfeeding is a frequent cause of illness in infancy. He would feed all normal babies not more than five times in twenty-four hours. I may say in passing that the dogma of four-hour feeding intervals is applicable in some cases and gives beautiful results. There are, however, babies who refuse to be satisfied, who thrive better on three-hour feedings, that is, six in the twenty-four hours. An open-minded physician will decide the question on the merits of the individual case.

Whole Milk.—The caloric value and the composition of cows' and breast milk are similar. A number of physicians have attempted to feed babies on boiled undiluted whole milk. Among these may be enumerated Budin, Variot, Bonnifas, Chavarne, and Rothschild, in France. In Germany the undiluted milk method has been practised by Schlesinger and Oppenheimer. Most pediatricians dissent from this plan of infant feeding.

The use of whole cows' milk is likely to produce disturbance of nutrition, especially if used before the fourth month. The baby should be gradually accustomed to this concentrated form of food, and, in any event, the quantity of whole milk used should be small. In the second month not more than $2\frac{1}{2}$ ounces should be given at a feeding, and in the third month not more than 3 ounces at a feeding; in the fourth and fifth month about 4 ounces in the feeding. It has been suggested that if the milk be boiled and be treated with pegnin or chymogen, whole milk can be consumed with less difficulty. The preparation of pegnin or chymogen milk will be described later.

Diluted Milk.—Various attempts have been made at different times to prepare cows' milk in such a way as to resemble mother's milk. Formerly it was thought that the casein was the indigestible substance in milk, and that it must be diluted in

cows' milk so that its 4 per cent. content could be reduced to 2 per cent. or less to resemble the 2 per cent. composition of mother's milk. As a matter of fact there are other substances in milk than casein which cause infinitely more harm than protein substance itself. It very often appears in feeding sick babies that substances which are the least like breast milk give the best results. It may be said that the attempts of the "alchemists" to make breast milk out of cows' milk, or even to make the one approximately the substitute for the other, especially in sick babies, have been far from successful. During the first months of life it is advisable to dilute the milk. It is questionable whether the mere dilution of milk favors its digestion, because after the ingestion of milk into the stomach the fluid portion is very soon separated from the curd. The great advantage of dilution is found in the fact that the desire for food and the feeling of hunger is satisfied by a larger quantity, and also that the danger of overfeeding is avoided. During the early months of life milk is diluted with plain water. Some of the older doctors used veal broth as a diluent. Monti diluted his milk mixtures with whey.

For young infants and the newborn, whole milk should constitute one-third of the mixture. In older children this proportion should be increased. One may proceed to one-half milk at two to four months, two-thirds milk at four to six months, and three-fourths milk at six to nine months.

Energy Value of Infant's Foods.—A normal baby shortly after birth should receive 45 calories of food for every pound of body weight, and this should constitute the quantity of the day's feeding. At the end of six months it should receive 38 calories per pound of body weight, and at the end of a year 32 calories. Premature infants require relatively larger quantities of food fuel, and if possible should be given 50 to 65 calories per pound of body weight. Budin estimated that a young infant should receive a quantity of milk equal to one-tenth of its body weight. In routine practice it is probably better to calculate that a child six months of age or under should receive 1½ ounces of milk for every pound of body weight. The weight of the infant should be considered about the number of pounds that a normal infant of the same age

should weigh. Thus, a child of three months that weighs only 8 pounds should be receiving as much food as would be given to a three months' old child with the usual weight of 11 to 12 pounds; that is, it may be necessary that he receive $15\frac{1}{2}$ to 18 ounces of milk in the twenty-four hours in order to gain in weight. Older children frequently will progress favorably with $1\frac{1}{4}$ ounces of milk for every pound of weight.

The following is a brief table of the caloric value per ounce of the more common food substances used in infant feeding:

Food.	Calories per ounce.
Cows' milk	21
Human milk	21
Skim-milk	11
16 per cent. cream	54
Buttermilk	11
Buttermilk mixture	21
Eiweiss milk	12
Chymogen milk	21
Keller's malt soup	25
Cane-sugar	120
Cereal waters	3
Milk-sugar	120
Dextrimaltose	110
Flour	100

It must be said that the process of calculating energy values of the infant's food is not a system of feeding. It must be regarded simply as a method of reckoning food values. It does not take into account ability of the infant to digest, nor does it consider the infant's tolerance for the individual components of the food. Babies who are receiving sufficient food to cover their energy needs or, indeed, who are receiving excessive quantities of food, may fail to gain in weight. This depends, however, upon some defective process of digestion or assimilation, or both, and this question will be referred to again when the subject of alimentary disorders is reached.

The estimation of caloric values of food may be applied to the percentage method of feeding, and in such cases a double calculation could be employed, the former to guide in the preparation of the food, the latter to estimate the fuel value.

In the **percentage system** of feeding babies, which is still extensively used in this country, the fat, sugar, and protein are varied in such a way as to meet the individual needs of infants and to permit such variations as the increased or diminished tolerance of the infants may require. The food is modified in such a way as to cause the milk preparation to resemble in some degree the chemical composition of human breast milk. This is usually done by dilution of the milk and the addition of cream and sugar. There is no doubt that in skilful hands this plan of feeding will prove successful in a certain number of cases. It is a plan of feeding which has its range of usefulness. It may be applied in feeding normal infants, but in order to apply this method, or any other method, intelligently one should have a definite idea of the physiology of the component food-stuffs and their action in health and disease.

Other food preparations besides cows' milk will be considered in the treatment of sick infants or those with diminished food tolerance.

The **carbohydrates** which come under consideration in the infant's diet are, first, the monosaccharids, such as grape-sugar and fruit-sugar, which occur in fruit and honey, and deserve consideration in older infants; second, disaccharids, such as lactose, cane-sugar, and malt sugar; and, third, the polysaccharids, such as flour, dextrin, cellulose. The latter occur in cereals, gruels, zwieback, and vegetables. These carbohydrates are split up by appropriate ferments, ptyalin, lactase, maltase, and invertin. They are absorbed as monosaccharids, and when they are carried out of the intestinal wall or after having been burnt and converted into glycogen they become stored as part of the organism. Some of the carbohydrates undergo fermentation as the result of the activity of intestinal bacteria, and these fermentations contribute toward normal as well as pathologic peristalsis of the intestine. Under normal conditions the fermentation causes an increased acidity of the intestinal contents, and in this way the increased peristalsis is brought about. This serves a useful purpose by removing the irritating substance from the bowel as soon as possible. Another vital activity of the acid produced by normal

fermentation is the aiding in the absorption of all of the inorganic salts. This is of special importance in the case of calcium, in that the acid medium prevents the formation of insoluble calcium soaps. The evidence all goes to show that lactose is absorbed more slowly than other members of the disaccharid group. It has been shown that lactose and maltose increase the retention of nitrogen, but apparently have no influence on the retention of ash or the absorption of fats.

Fats.—The first step in fat digestion consists of its emulsification and splitting up, so that the resulting fatty acids combine with the alkaline secretions of the intestines, and in this way are to a large extent absorbed. The alkali in a free state is again given off at the moment of passing through the intestinal wall, so that it may again combine with the fat. A small portion of the fat is found in the stool, either as neutral fat or else as free fatty acid, or in the form of potassium or calcium soap.

Fat absorption in healthy infants is very high, both on breast milk and on cows' milk. In artificially fed babies, even those who are not gaining in weight or who are suffering from nutritive disorders, fat absorption goes on to a high degree.

Czerny has maintained that an increase in the amount of fat in the food will cause eczema. Students of children's diseases have come to the conclusion that excessive fat, either in breast milk or cows' milk, may be the source of digestive disturbance serious in character. It must not be forgotten, however, that the normal breast-fed baby is receiving considerable fat and that a large number of artificially fed babies can digest a reasonable amount.

Metabolism of the Salts.—So far as salts are concerned, the alimentary tract serves not only as the place for absorption, but to a less degree for elimination. For example, calcium, magnesium, and iron to a considerable quantity are found in the stools.

Human milk contains more salts than are required by the infant, but the supply of iron is just sufficient. In cows' milk there is about four times as much mineral matter as in human milk and the supply of iron is very low.

The absorption and assimilation of calcium present a very complicated process. Calcium is lost to a large extent through the feces, in greater amount in artificial feeding than in breast feeding. It has been suggested by one of the recent investigators that calcium retention is better obtained with high fat feeding than with low fat feeding.

The Protein of Cows' Milk.—The older authors laid stress on the injurious effects of the protein of cows' milk. A definite reaction in thought has occurred among more modern writers and opinions have very materially changed. The protein is thought to contribute very little, if any, toward the disturbances of digestion and nutrition.

It has not been definitely shown by recent investigations that casein participates in the alimentary disturbance. Indeed, it has been shown that if larger quantities of casein be administered acid fermentation will be inhibited. In contradistinction to the above is the view of Vaughn that peptone and other decomposition products of proteins cause symptoms of disease, and that sensitization may result from the absorption of undigested or partially digested protein from the alimentary tract.

The protein after it has passed the intestinal wall has three important functions: (1) To supply the loss of protein substances. Protein is lost by the desquamation of epithelium, the loss of hair, and perspiration, the production of digestive secretion, and also through the nitrogen given up by all cells during their activity. (2) To satisfy the needs of growth. It would be impossible for cell growth to occur without albumin. (3) Protein assists in restoring the energy which is lost by heat production. It follows that protein is a necessary article of diet; a continuous supply is required by cells in their metabolic function and it is necessary for all the vital processes. The protein under the influence of the digestive ferments is split into the amino-acids and other protein end-products. It seems to make no difference from the standpoint of the infant's nutrition whether the protein be derived from human milk or other milk. In either case the protein molecule must be split before it can combine organically with the cell. The end-products of protein metab-

olism as they occur in the urine may be identified as urea, ammonia, uric acid, and creatinin. The nitrogen that is found in the feces is derived either from the intestinal secretions or bacteria, much less than from the food.

To recapitulate: Protein is a necessary article of food for growth and for carrying on physiologic functions of the body. It may be concerned in heat production; it is supposed to inhibit fermentation, and recent investigators claim that protein participates slightly if at all in alimentary disturbances, though Vaughn sees in the protein element a cause for profound alimentary disturbances in infants.

Let us take a few concrete examples: A child three months old, weighing 11 pounds, has been weaned from the breast. Estimating that the baby would require $1\frac{1}{2}$ ounces of whole milk for every pound of weight, the mixture would require $16\frac{1}{2}$ ounces of milk. Now, if this baby were to receive six feedings of $4\frac{1}{2}$ ounces each the baby would require 27 ounces of food, of which $10\frac{1}{2}$ ounces would be water and $16\frac{1}{2}$ ounces cows' milk. Five per cent. of sugar may be added to this mixture and we may use dextrimaltose as the carbohydrate addition. We may calculate that the $16\frac{1}{2}$ ounces of milk would supply $346\frac{1}{2}$ calories; $1\frac{1}{4}$ ounces of dextrimaltose, being the 5 per cent. of sugar added, would represent $137\frac{1}{2}$ calories. The mixture then would equal 484 calories, which will equal 44 calories per pound.

One may find after several days' trial that the baby shows some intolerance or that he refuses to gain in weight. If the stools should be diarrheal, we will be tempted to diminish the sugar; if he fails to gain in weight, though the stools are normal and the baby seems happy and contented, more carbohydrate may be added or a very slight increase in the quantity of fat might be cautiously attempted.

Let us prepare a formula with $3\frac{1}{2}$ per cent. of fat, 6 per cent. of sugar, and $1\frac{1}{2}$ per cent. of protein. Multiplying the percentages by 27, the product equals 94.5 parts of fat, 162 parts of sugar, and 40.5 parts of protein. Constructing an equation, you have—

16 cream plus 4 milk equals 94.5;
4 cream plus 4 milk equals 40.5.

Reducing to the least common denominator:

4 cream plus milk equals 23.6;

cream plus milk equals 10.1.

Subtracting:

3 cream equals 13.5.

Cream equals $4\frac{1}{2}$ ounces, and the milk is the difference between $4\frac{1}{2}$ and 10.1.

Subtracting the quantity of cream to be used in the mixture from the milk quantity in the equation, we find that the mixture will require:

$5\frac{1}{2}$ ounces of milk;

$4\frac{1}{2}$ ounces of cream;

and, since the sugar represents 162 parts, approximately 1.6 ounces.

Now, figuring the caloric value of the above mixture, we find:

$4\frac{1}{2}$ ounces of 16 per cent. cream at 54 calories per ounce equals 243 calories;

$5\frac{1}{2}$ ounces of milk, 115.5 calories;

$1\frac{1}{2}$ ounces of sugar, 165 calories;

Total, 523.5 calories, or 44 calories to the pound weight.

Thus we see that the energy needs of the infant are covered, and providing the baby shows no intolerance for the fat content of the food, no reasonable objection could be urged against its use.

The physician of experience, whether he be surgeon, obstetrician, or a practitioner treating children, adopts the simplest methods. Personally, it is my own conviction that the simple whole milk dilutions are to be chosen because they are simplest to calculate, more readily prepared in the home, make more complete emulsions, and are in a large percentage of the cases adequate food mixtures. The danger of fat overfeeding is avoided and the energy requirements of the infant, so far as we understand them, are complied with.

Let us take another example of a baby, six months' old, weighing 15 or 16 pounds. Such a baby could possibly take 7 ounces at a feeding and receive five feedings per day (that is, fed at 6 A. M., 10 A. M., 2 P. M., 6 P. M., and 10 P. M.). Calculating that he

would receive $1\frac{1}{2}$ ounces of milk per pound of weight, the mixture would require 24 ounces of milk and 11 ounces of diluent (the diluent in this case might very well be a 3 or 5 per cent. cereal water) and $1\frac{3}{4}$ ounces of dextrimaltose.

Calculating the caloric value of this mixture—

24 ounces of cows' milk is 504 calories:
$1\frac{1}{3}$ ounces of sugar equals 192 calories;
$\frac{1}{3}$ ounce of barley flour equals 33 calories.
Total, 729 calories, or about 45 calories per pound.

If we apply the percentage system to the same mixture, advising a formula of 4 per cent. fat., 7 per cent. sugar, and $2\frac{1}{4}$ per cent. protein, we may ascertain that the mixture will require 5 ounces of 16 per cent. cream, 14 ounces of whole milk, 2 ounces of sugar or dextrimaltose, and $\frac{1}{3}$ ounce of cereal flour.

If one checks this up by estimating caloric value it will be found that the mixture contains 817 calories, or about 51 calories per pound of baby's weight.

This mixture, then, is excessive of the baby's nutritional needs as we calculate them, though the caloric value may be reduced considerably by diminishing the amount of sugar and omitting the cereal flour.

PREPARATION OF INFANT FOODS

Dr. Abt: I shall now ask Miss B. E. Wilson, the dietitian in the milk kitchen, to demonstrate the preparation of some of the foods which we use for the infants in health and disease.

Miss Wilson: *Saccharin Water.*—To 1 quart of sterile water add a scant teaspoonful of table salt. This may be boiled. To this add $\frac{1}{2}$ to 1 grain of a saccharin tablet.

Tea.—One-half teaspoonful is steeped with 8 ounces of water, and then enough water is added to make 1 quart. This mixture should have a yellowish-brown color. Saccharin is added to sweeten.

Flour ball is made by taking 1 pound of wheat flour, placing it in a sterile muslin bag, dropping it into a pail of hot water, and allowing it to boil for eight hours. At the end of this time it is taken out of the sack, and it presents itself as a compact mass

with a crust on the outside about $\frac{1}{4}$ inch thick. This crust is peeled off, and in the interior of this mass is a hard dextrinized flour. It may be placed all night in an oven that has been heated during the day, leaving the oven-door ajar. The dextrinized flour may be pounded in a mortar, but we have found it better to put it in a "Nixtamal mill," made by the Enterprise Manufacturing Company, and ground into a fine powder. It may then be passed through a sieve, and then it has the appearance of ordinary flour, though it has been dextrinized.

We use flour ball for making cereal decoctions for young infants; to increase the carbohydrate content of the milk preparation; likewise in the preparation of Eiweiss or albumin milk.

Dr. Abt: Miss Wilson will now describe the preparation of *Eiweiss*, or *albumin milk*, as advised by Finkelstein and Meyer, which is largely used for feeding sick infants, or, to use the technical expression, for the purpose of detoxicating the babies who are suffering from food injuries.

Miss Wilson: One quart of whole milk is heated until it reaches a temperature of 104° F. At that temperature add 2 teaspoonfuls of chymogen powder (Armour & Co.) or essence of pepsin or rennet ferment first dissolved in a little water. The mixture is now placed in a water-bath at a temperature of 107° F. for fifteen to twenty minutes until coagulation occurs. The curd separates from the whey. The whey is then poured off and thrown away. The remainder of the curd mixture should then be placed in a sterile muslin bag and suspended and allowed to drain. The dry curd thus obtained may be mixed with a pint of buttermilk and rubbed through a fine sieve or a copper gauze strainer three times. In place of this, however, we are at present grinding the curd with the buttermilk through the Nixtamal mill, which is rapid, efficient, and labor-saving. Then one or two teaspoonfuls of flour ball or white flour are thoroughly mixed with 1 pint of water. This latter is then added to the curd and buttermilk mixture. The mixture is now placed upon a slow fire and allowed to boil for ten minutes, stirring it constantly with a large wooden spoon so as to avoid the formation of large curds. Water should be added to make the finished mixture 1 quart.

Buttermilk mixture consists of mixing cane-sugar, wheat flour, or flour ball and fat-free or churned buttermilk. To $2\frac{1}{2}$ level teaspoonfuls of flour add enough buttermilk to make 1 quart. Bring it to a boil three successive times and remove from the fire after each heating. Before the third boiling add 1 ounce of sugar. The preparation of the mixture requires about twenty minutes. Add enough water to make 1 quart to supply that which is evaporated. This mixture is low in fat, high in carbohydrates.

We use two buttermilk mixtures, suggested by Dr. Jules Brady, of St. Louis: *Mixture No. 1* consists of 24 ounces of skimmed buttermilk, 8 ounces of barley gruel (1 ounce of barley flour) and 8 ounces of water, 1 ounce of Mellin's food, $\frac{1}{2}$ ounce of cane-sugar. The ingredients are mixed together in the following manner: To the barley gruel is added the cane-sugar and the Mellin's food, and then the buttermilk is slowly added and the mixture strained. Note that the buttermilk is not boiled. The mixture is rather thick and has the sour taste of buttermilk.

Mixture No. 2 may be used for older children, and is made by using $21\frac{1}{3}$ ounces of whole acidified milk, that is, whole milk that has been soured by addition of lactic acid ferment, $10\frac{1}{3}$ ounces of barley gruel, and 1 ounce of cane-sugar.

Keller's Malt Soup.—To 11 ounces (330 gm.) of warm milk gradually add $1\frac{2}{3}$ ounces (50 gm.) of flour, stir constantly, then pour through a clean wire or muslin sieve. In another dish dissolve 3 ounces (100 gm.) of Löfflund's or Borcherdt's malt soup extract in 20 ounces (600 gm.) of boiled warm water. Then mix both solutions, put on the fire, stir continually, and boil for two or three minutes.

Larosan milk is made by adding whole milk to larosan powder. The mixture is prepared as follows: Two-thirds of an ounce of the larosan powder is added to $\frac{1}{2}$ pint of milk and mixed thoroughly. Another whole pint of milk is heated to the boiling-point. When it has come to a boil it is added to the larosan milk mixture, and the whole is placed on the flame and allowed to boil for five minutes. This may be diluted with water in the proportion of one-half larosan milk and one-half water, or two-thirds larosan milk and one-third water. In passing, I may say

that the larosan powder is a soluble calcium casein and consequently increases the casein content of the food.

Chymogen or Pegnin Milk.—Boil milk for five minutes, cool to 104° F., add one full teaspoonful of chymogen or pegnin to each quart of milk, and stir for one-half minute. Let it come to a clabbard by allowing it to stand for fifteen minutes, then beat it well until the curd is finely divided. Do not heat above 100° F. when preparing individual bottles for feeding.

Cereal pudding for older children. To about 3 ounces of milk add 1½ teaspoonfuls of a fine cereal (farina, cream of wheat, or cornstarch); pinch of salt is added, and the whole is allowed to boil in a double boiler for about one-half hour. In the same way rice, sago, tapioca, oat flour, or barley flour may be used. The above is a 7 per cent. mixture and has the consistency of a thick soup. The 10 to 12 per cent. mixture has the consistency of a stiff pudding.

Dr. Abt: At another period I propose to give more definite directions concerning the therapeutic indications for the use of the food preparations above enumerated, and to point out methods of administration and their application in alimentary disorders.

CLINIC OF DR. RALPH C. HAMILL

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

AN UNUSUAL CASE OF MULTIPLE SCLEROSIS

Exaggerated Voluntary and Involuntary Movements, with Scanning Speech and Lost Abdominal Reflexes. Onset Four Years After Attack of Chorea. Pathology of Multiple Sclerosis. Probable Hematogenous Origin.

THIS patient is of unusual interest because of the variety of abnormal muscular movements, voluntary and involuntary, that she shows. Upon attempting voluntary movements there are marked abnormalities seen in the execution of the movements, such as might be ascribed to a very advanced stage of multiple sclerosis. There are also movements while at rest suggesting some other condition, or at least some very unusual combination in multiple sclerosis.

It has been justly said that the unusual cases of multiple sclerosis are quite as important and form quite as large a category as the normal cases, that is, the cases showing merely the pathognomonic symptoms—the intention tremor, spasticity, nystagmus, and emotional disturbances. The fact that there are such a large number of unusual cases of multiple sclerosis is readily understandable when one appreciates the fact that the symptomatology of the cases depends entirely, or at least very largely, upon the particular distribution of the plaques of sclerosis occurring in any given case.

Pathology.—The essential lesion of multiple sclerosis consists of a patch of glia fibers and glia cells, located at any point in the central nervous system, varying in size from the diameter of a millimeter to the diameter of a centimeter or more. Although usually fairly regular in outline, it may not be so, owing possibly

to the original formation or possibly to the coalescence of two or more plaques. These sclerotic plaques composed, as I say, of glia cells and fibers, seem to have, at least in the majority of cases, a fairly definite relationship to the blood-vessels. In many cases a blood-vessel is found near the center of the plaque showing some change in its wall which varies from slight infiltration to thrombosis. This, of course, suggests the hematogenous origin of the noxious agent causing the plaque.

Furthermore, it is probable that the first change in the plaques consists in an acute inflammatory or, perhaps more correctly, an acute degenerative destruction of the myelin sheaths of the particular locality. One is justified in saying this because in these plaques we occasionally find droplets of myelin in the bodies of glia cells or other phagocytic cells. Also, the marked characteristic of these plaques is the complete destruction of the myelin sheaths, as shown by a failure to stain in Weigert-Pal preparations. This failure to stain, or this destruction of the sheaths, is most marked at the center of the plaque; its intensity extends over a large portion of the plaque, but at the periphery the destruction gradually gives way to more normally reacting myelin sheaths.

The destruction of the myelin is further emphasized by the fact that in the centers of the plaques, and more truly away from the centers, the axones may show no change. In fact it was at one time claimed that the *axones were unchanged*. This can no longer be claimed, however, as I have several times seen in pathologic preparations a complete destruction of many axones near the center of the plaque.

This in a general way is a description of the characteristic lesion of multiple sclerosis. As I have hinted, it is probably of hematogenous origin. It is characterized by destruction of myelin sheaths, to a less degree of axones, and a replacement in the nature of a scar process of these parenchymatous structures by neurolgia. These plaques may occur at any spot in the central nervous system. They are seen in the optic nerve, even in the disc. They are seen in all parts of the brain and in any level of the midbrain, medulla, or cord.

Now, because the destruction is one largely of myelin and but slightly of axone, we get disturbance of function rather than loss of function. Consequently, paralyses, motor or sensory, are the exception. Abnormalities of function are the rule. This case shows this to an exquisite degree. One cannot say that there is a paralysis of any function. Many functions, however, are so changed as to be almost without service to the patient; that is, her control of her legs is so poor that although she can make movements in any direction of a fair degree of strength, the movements are so inco-ordinated that it is practically impossible for her to walk unsupported.

Her history is as follows: She is twenty-seven years old. She was married seven years ago, living with her husband only about a year; there was no pregnancy. She has a younger sister who had chorea at fifteen and recovered in about a month. There is an older sister and a younger brother who are quite well. A brother and a sister died from accidental causes in childhood.

You will remember that I said there was a younger sister who had chorea at fifteen; the patient also had chorea at fifteen, and this is a fact which I should like to discuss for a few moments. Chorea, as you know, is characterized by abnormalities of movement while the patient is at rest. These movements may subside or at least be slightly less marked when the patient attempts voluntary movements, or they may be intensified. They are almost always intensified by any emotional excitement.

These movements are due to an acute inflammatory process occurring in the brain, probably caused by a streptococcus. Dr. Rothstein and Dr. Rosenau have produced typical chorea in dogs and recovered the streptococcus from their brains.

Now, this patient at the age of fifteen had chorea, which came on suddenly, lasted a short time, improved, relapsed, improved, relapsed a second time, and cleared up at about the end of the year. Then for two years she was reasonably well. At the end of that time, however, she was seen by Dr. George Hall, who diagnosed multiple sclerosis because of her intention tremor and brisk reflexes. At that time she was a telephone operator, and her chief difficulty was that she was unable to plug the con-

nections because of the tremor. I saw her about that same time, and remember that the intention tremor and spasticity were fairly striking, and that there was about the same degree of nystagmoid movements in the extreme lateral positions that there is at present.

She improved somewhat after the disease began, then became worse very gradually, and in the past eight years her course has been gradually downward, with occasional periods when the disease process seemed to stand still. The difficulty with arm movements gradually became more marked and after a year or two involved also the legs. As the legs became worse, walking became more and more difficult, until at the present time she is unable to walk without support. In fact, it is only with great difficulty that she is able to stand alone. Her speech, as you hear, is distinctly syncopated, has been affected for several years, and now is fairly characteristic of a high degree of "scanning speech."

For the past year or two she has frequently urinated involuntarily during her sleep. Recently she has been having what have been described as epileptiform attacks. During the attack she is unable to move or to talk, though she says she does not loose consciousness and hears all that is going on around her. The attacks frequently come on as she is awakened. In the attack she may pass her urine involuntarily. As she says, the attack consists chiefly of a sensation of stiffness that comes on suddenly.

Physical Findings.—The patient is a rather thin, intelligent-looking woman. You are immediately struck by the involuntary, almost continuous movements of the right shoulder—a to-and-fro movement of the shoulder girdle, carrying the arm backward and forward at the rate of one to four movements a second. You notice that she is lying with her right hand under her hips and in spite of this the movements continue.

(To Patient): Why do you lie on your hand that way?

PATIENT: Because if I don't the movements get worse and my arm tires out up here (placing left hand on right biceps).

DR. HAMILL: As we take her right hand out from under her you see the movements become enormously exaggerated and involve the entire right upper extremity. You also notice that

she is lying with the left foot crossed over the right, and that when the movements in the arm become very marked there are synchronous flexion and extension movements in the leg. Lifting her left leg off of the right increases these movements in the same way that removing the hand from under the hips increases the movements in the arm. When the arm and the leg are both freed from their restraint the movements become so violent that they seem to communicate themselves to the trunk, and there are these same rapid jerkings of the entire right side of the body, extending to the muscles of the trunk, the back, and the abdomen.

In attempting the finger-nose test or the heel-knee test with the left extremities you see this very marked ataxic movement; at least it is so extensive that it is difficult to speak of it as a tremor. Rather it seems like an ataxic movement. As the hand starts moving toward the nose, the arm is agitated by these enormous variations from the direct movement to such a degree that she slaps herself in the face, or her hand hits on her chest far from the desired goal. Then, with her hand resting on her chest, she can approach her finger to her nose, though the same incoordinate movements are seen in the outstretched finger and hand in a lesser degree.

When we sit her up in a chair you see this rapid to-and-fro movement of the trunk, caused apparently by the contraction and relaxation of the posterior or dorsal flexors of the right thigh. You notice how much this is increased when some voluntary act is attempted.

(To Patient): Now squeeze my hand with your left hand. (Patient attempts to do so.)

You see how this exaggerates the rapid oscillation of the entire body, especially the extremities of the right side.

Her gait is even more affected. It is possible for her to walk only when she is supported from one side as well as by the nurse's arm around her. The left leg advances, jerkily to be sure, but fairly efficiently. The right, however, is thrown outward in the arc of a circle, jerking once or twice in its forward course, is stamped down on the floor, and then as she transfers her weight on to the right foot there is a rapid pronation and supination at

the ankle-joint, so that first the internal malleolus and then the external malleolus hits the floor. Along with these movements of the ankle-joint there are the rapid oscillations of the knee- and hip-joints. The hip passes backward and forward in time with these oscillations, violently agitating the whole body.

Therefore, we have here inco-ordinated, tremor-like movements in the right arm and right leg at rest. These movements are much exaggerated as she attempts voluntary movements. The same abnormalities are present on attempting movements in the left arm and leg, though to a lesser degree. On the left side, however, there are no movements while at rest.

There is practically no nystagmus, merely faint nystagmoid twitchings in the extreme lateral and upward positions. The pupils respond perfectly to light and accommodation, facial innervation is symmetric and normal, and the optic nerves are apparently normal. The tongue protrudes normally; sensation seems undisturbed. When it is possible to get relaxation of the muscles, the Achilles and patellar reflexes are brisk on both sides. The plantar reflexes are reduced, especially the right, but otherwise are normal. The abdominal reflexes are lost.

Diagnosis.—This case, then, shows a tremor or inco-ordination which appears with voluntary movements. It is present on the right side when at rest. There is a scanning speech and the reflexes may be spoken of as increased, though that is not always demonstrable. The abdominal reflexes are entirely absent. There is failure of control of the bladder function. As you have seen in the examination, she is very quick to change in her emotional responses, suggesting at least spasmodic laughing and crying, which is spoken of as a frequent symptom of multiple sclerosis. Mentally, there is no demonstrable impairment.

This disease came on at the age of nineteen, four years after chorea—an inflammatory disease of the central nervous system. As I have implied in my description of the pathology of multiple sclerosis, it must be considered, at least in many instances, as the result of an acute inflammatory process. Consequently, I am inclined to say that multiple sclerosis is as good a definitive term as we can use in the case of this patient. She is especially inter-

esting because of the occurrence of the acute chorea. The movements involving the right arm and leg suggest the movements seen in progressive lenticular degeneration. At times the fingers and thumb of the right hand are agitated by a slow rhythmic tremor suggesting that of paralysis agitans. The blood and spinal fluid have been uniformly negative.

I am inclined to call this multiple sclerosis for the following reasons: It came on in the latter part of the second decade, the usual time for the onset in multiple sclerosis. The course of the disease has been gradually downward with periods of arrest, also characteristic of multiple sclerosis. Of the essential symptoms of multiple sclerosis she shows the disturbance of voluntary movement, lost abdominal reflexes, and scanning speech, perhaps also slight emotional instability.

Added to the usual symptoms of multiple sclerosis are the choreiform movements of the right arm and leg—movements almost constant during rest, and immensely exaggerated during voluntary use or when the limb is free to move without such restraint as keeping the left leg over the right or lying on the right hand.

These movements in their time suggest the movements seen in *progressive lenticular degeneration*. Hence, I would be inclined to suspect that they are due to the presence of plaques in the lenticular nucleus, and very possibly these plaques are breaking down, as collections of neuroglia have a tendency to do. Consequently, it is my opinion that there is a progressive lenticular degeneration going on in this case, in the left lenticular nucleus especially. If such a degeneration is occurring, this case may serve to link together the three processes—acute chorea, multiple sclerosis, and progressive lenticular degeneration.

It is interesting to note that pus could be extracted from both tonsils. On May 3d her tonsils were removed on the theory that this tonsillar infection might have some etiologic influence on the present disease, inasmuch as we know that acute chorea frequently follows tonsillitis. She has received a few injections of a culture made from the bacteria isolated from the right tonsil. I have very little confidence in the efficacy of this treatment; it is merely used as the only thing we have to fall back on.

EXTERNAL OPHTHALMOPLEGIA DUE TO DISEASE OF THE PONS

Wide-spread Symptomatic Changes Due to a Lesion of the Pons, Involvement of Cranial Nuclei and the Pyramidal Tract.

THIS patient I saw first in the ophthalmologic ward about a month ago. At that time there was a complete paralysis of all the muscles of the left eye except those controlling the sphincter of the iris. There was a ptosis with complete inability to raise the upper lid, the eyeball moved in no direction whatsoever, but the sphincter of the iris retained its function. The left pupil was small, smaller even than that of the right eye. There was also a diminution of sensation of the left cornea. I merely saw the man in passing, without having time to examine him, and did not notice a paresis of the right side of the body. At the time I thought the disease was possibly in the left orbit and requested an *x*-ray made of that region. A subsequent examination showed the uselessness of that procedure, since it discovered symptoms indicating disease of the pons in such a location as to account for the symptoms in the muscles of the eye. It is very difficult to obtain any history because of the combination of slight deafness and extensive stupidity.

The patient is a Scandinavian, sixty-seven years of age. Several months ago he was operated for a large, fluctuating swelling over the right mastoid. Three months ago he developed pain in the left brow, the left side of the head, and then gradually lost the power to raise the left upper lid. Further facts in his history are too indefinite to be dependable.

Examination reveals a paresis of the right side of the body. He scrapes his right foot as he walks, his foot sticks to the ground, and the leg as it moves forward is abducted, suggesting the spread of the feet seen in cerebellar ataxia. As he walks the right arm is

held against the side of the trunk down to the elbow; from there it is abducted and the hand takes a peculiar spasmodic position strongly suggestive of that seen in athetosis. The thumb and forefinger are extended, the last three fingers flexed in their proximal phalanges. This position of the hand is changed in an athetoid manner whenever he is on the move (Fig. 45, *a*, *b*, and *c*). When he attempts to grasp objects with his right hand he spreads the fingers and slightly overextends them, especially the fourth and fifth, and the hand and fingers go into slight ulnar flexion. Voluntary movements of the right arm and hand are weaker than those of the left, though the difference is not marked. There is slightly more resistance to passive movements in the right arm and leg than in the left.

Reflexes.—Tapping the flexor tendons at the wrist causes a sharper jerk on the right side than on the left, but below the lower end of the radius, where we ordinarily obtain the wrist-jerk, the reflexes are only barely demonstrable. The biceps and triceps reflexes are brisker on the right side than on the left; the right knee-jerk is brisker than the left. Even with good relaxation of the muscles of the calf, such as one may obtain by having the patient lie on his stomach with the legs flexed at the knee, the Achilles reflexes are not demonstrable. The left plantar reflex is not frank, but is usually normal. The right shows a hammer-toe and no plantar reflex. Occasionally there is a rather coarse tremor affecting both the right arm and leg. The abdominal reflexes are diminished about equally; the cremasterics are normal. There is no Beevor sign. The right rectus abdominalis muscle seems to be stronger than the left. In attempting repeated pronation and supination, as in testing for diadokokinesis—*i. e.*, good control or good functioning of the cerebellum—there is a marked clumsiness in the movements of the right arm and hand.

The right-sided hemiplegia is not of marked degree. There are slight differences in the reflexes which are brisker on the right than on the left; there is pronounced clumsiness in the right arm and hand, a gait which shows less sense of certainty in the right leg than in the left, with the right foot sticking to the ground and scraping more than the left. There is also a little less strength

a

b

c

Fig. 45.—Right hand, showing athetoid movements which accompanied forceful voluntary movements of the left arm.

manifested in the extremities of the right side than in those of the left.

Slight as these symptoms are, they nevertheless indicate interference with the function of the pyramidal tract somewhere above its decussation or at least very high in the cervical cord. When we study his face carefully we see that the nasolabial fold on the

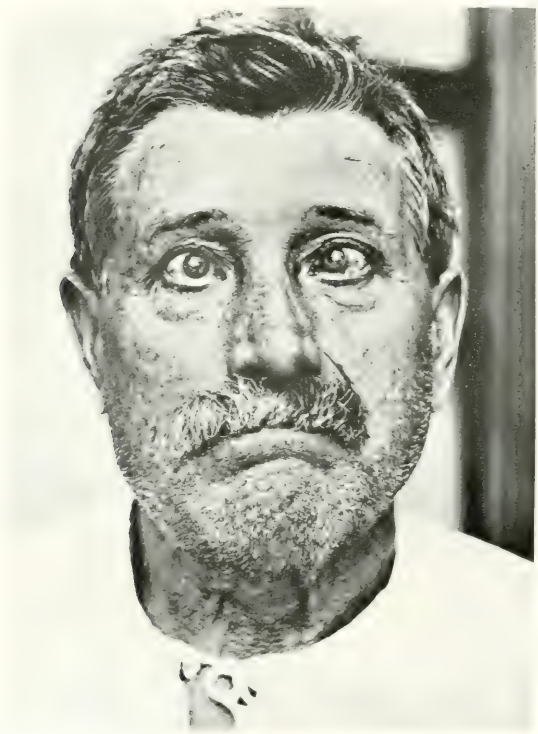

Fig. 46.—Shows the turning in of the left eye, the ironing-out of the right nasolabial fold, and the drooping of the right angle of the mouth.

left side is definitely deeper and more marked than that on the right (Fig. 46). The right side of the face has a rather ironed-out look, as though the wrinkles had been obliterated from that side. Even those above the eyebrows in the forehead are a little less deep on the right side than on the left. When he attempts to make voluntary movements with the face, as in showing his

teeth and in protruding the tongue, there seems to be more movement on the right side than on the left (Fig. 47). I think this apparent difference is due in part to the fact that the right end of the mouth hangs lower and more forward, so to speak, than the left. Consequently, its excursion seems greater. In attempt-

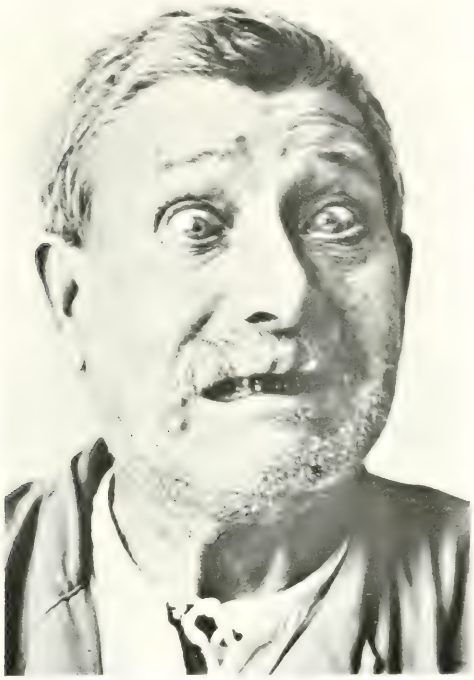

Fig. 47.—Shows the effect of patient's maximum effort to draw back the angles of the mouth. The movement of the sides is approximately equal. The exaggerated opening of the right eye is noteworthy.

ing to show the teeth his mouth forms itself much in the shape of an exclamation point, with the larger portion to the right.

The ptosis seen in the first examination cleared up in about three weeks. At the present time there is marked internal strabismus of the left eye. He can move it outward almost to the middle point, but not beyond. Movements upward and downward are approximately normal, and inward are very good.

In other words, the complete ophthalmoplegia which existed when I first saw him has given way, leaving a paralysis of the abductor, the sixth nerve.

As I said, there is some deafness. This is more marked in the left ear than in the right, though the mastoid operation performed about five months ago was on the right side. This deafness in the left ear includes both air and bone conduction. The Weber test is lateralized in the right ear. Bone conduction transmits vibration equally to the two ears, but it is appreciated better on the right side than on the left. Consequently, we must assume that the right auditory nerve is functioning better than the left. In other words, the left auditory nerve—the eighth nerve—is also involved. When we test the ears by irrigation with cold water, the Barany caloric test, we find approximately equal response from the two ears, except that the response from the right ear is stronger than that from the left; that is, there is a diminution of function on the part of the vestibular apparatus rather than a change of function.

General examination reveals a high degree of arteriosclerosis. His radials and brachials feel like a chain of beads. Lumbar puncture done on May 25th revealed thirty cells to the cubic millimeter and an increase of globulin content. The Wassermann reaction, however, was negative. The Wassermann reaction on the blood on May 12th was positive; on the 25th it was negative. In other words, we cannot depend much upon the Wassermann.

In a man of his age and with his arteries we must conclude that we have here a group of symptoms depending upon arteritis of the vessels coming off from the circle of Willis. The commonest causes of such a vascular disease are a rheumatoid diathesis and syphilis. In favor of the latter is the Wassermann of May 12th. Whether all the symptoms are due to a single lesion, or whether there are multiple lesions, is difficult to determine.

We cannot get a history of even one attack, let alone two, coming on in such a manner as to show with certainty that attacks have occurred. In other words, the history does not help us at all; we have to depend entirely upon symptomatology.

First of all, I should like to enumerate the symptoms once

more, and will do so in the order of their sequence in the central nervous system; that is, beginning with those due to the centers nearest the brain and proceeding caudalward down through the midbrain.

There was a ptosis and a paralysis of all the external muscles of the eye. This meant an involvement of the third nucleus, excepting only the fibers controlling the pupil, the fourth nucleus, and the sixth nucleus. There is some deafness of both ears, but

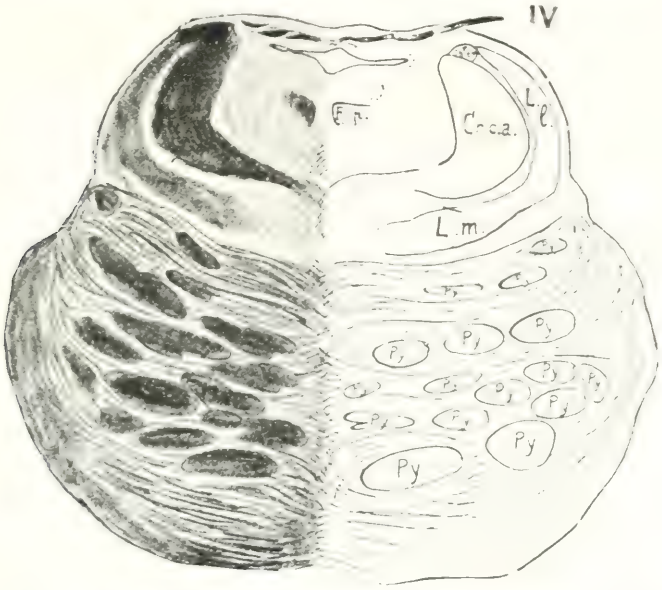

Fig. 48.—*Cr.c.a.* contains fibers running from cerebellum to red nucleus, part of accessory motor tract. The proximity of the fibers of the fourth nerve (IV) to both this accessory and to the primary motor tracts (*Py*) is apparent.

perhaps more marked on the left side, indicating a certain amount of interference with the impulses from the eighth nerve.

This category includes the disturbances due to interference with the nuclei of the cranial nerves.

The athetoid clumsiness of the right hand I would ascribe to interference with the fibers running in the superior cerebellar peduncle from the cerebellum to the red nucleus, whence they run upward to the cerebral basilar ganglia, the optic thalamus, and

lenticular nucleus. This tract of fibers constitutes an accessory motor tract in the sense that interference with its function shows itself by a failure of perfect control of movement and disturbed control of tonus. At least some if not all of the cases of athetosis occurring in adults are due to interference with the function of this tract. If you will look at this chart you will see that the fibers of the superior cerebellar peduncle are not at a great distance from the oculomotor nuclei (Figs. 48 and 49).

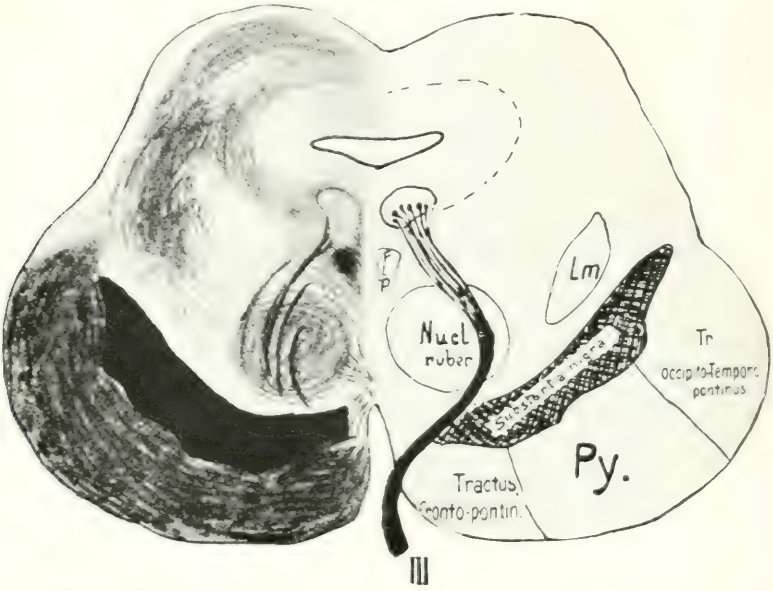

Fig. 49.—The fibers of the oculomotor nerve, the third, are shown passing through the red nucleus (*Nucl. ruber*), a part of the accessory motor tract.

The increased reflexes and the slight weakness shown in the right extremities and the ironed-out appearance of the right lower face indicate an interference with the function of the pyramidal tract in the left side of the midbrain above the point where the fibers decussate to the facial nucleus; that is, the pyramidal tract in the lower half of the pons. Reference to this chart shows you how a single lesion could involve the cranial nuclei and the pyramidal tract at the same time (Figs. 48 and 49). That the eye, which previously was entirely stationary, should now be turned

in does not necessarily mean that the sixth nucleus is affected to a much greater degree than the third. The fact that the eye is constantly turned in and can be abducted only to the middle line does, to be sure, show that the muscles innervated by the third nerve are capable of more powerful action than that innervated by the sixth. However, it is known that primarily the muscles of the third nerve have a much greater power than that of the sixth under normal conditions. You may remember a patient whom I showed you a year ago who had a complete paralysis of the oculomotor nerves of both eyes. The first evidence of improvement with him was a turning in of the eyes; that is, the third nerves acquired sufficient strength to move the eyeballs inward before the sixth had developed sufficient strength to counteract the third. So in this case it may very possibly be that the turning in of the left eye is evidence of the third nerve's inherently greater functioning power rather than that the third nerve has recovered and the sixth has not. Further progress in this case may show a return of function of the sixth.

In the part of the central nervous system in which we assume this disease process to be it does not require a large lesion to produce wide-spread symptomatic changes. The cranial nuclei and the pyramidal tract can easily be caught at the same time. Consequently, I think that we can assume a single vascular process, or a disease of a single vessel, as the causative factor in the production of the major part of this man's symptomatology. The loss of the ankle reflexes is probably evidence of disease in the lower spinal cord. The combination of the pontine lesion and this lower cord disturbance is evidence in favor of the syphilitic origin of the arteritis.

Treatment.—This man's age, his habit of life, and lack of care of himself all count seriously against the efficacy of antisyphilitic treatment. Mercury, however, has been given him, and while he has been rubbing a dram a day of blue ointment into his skin there has been considerable improvement. That this improvement is due to the treatment does not necessarily follow, however. A high degree of atheroma of the blood-vessels forestalls the probability of complete return of function.

It is impossible to saturate him with mercury. His teeth, as you see, are in frightful condition, and have been ever since his first entrance into the hospital. Their present condition is not due primarily to mercury. Arsenic would be the drug of election in his case. Unfortunately, in the County Hospital it is impossible to obtain the newer arsenic preparations *ad libitum*, so we will go on with a small amount of mercury and saturated solution of potassium iodid.

PRESENTATION OF A CASE OF PROGRESSIVE MUSCULAR ATROPHY DUE TO SYPHILIS OF THE ANTERIOR HORN CELLS

Differential Diagnosis From the Progressive Muscular Atrophy of Charcot, Syringomyelia, and the Myopathic Atrophies.

THIS patient is an example of a form of syphilis which is unusual and which was not recognized previous to the last seven or eight years. He suffers from a form of syphilis attacking the parenchyma of the central nervous system rather than the meninges or blood-vessels. It is a disease of the anterior horn cells; at least the great preponderance of symptoms is due to the destruction of these cells.

Present History.—The patient is a single man, forty-three years of age. In 1894 he had a chancre. Two months later he was circumcised and was given some pills and a tonic for four months, after which he was discharged as cured. He has had no further treatment.

In August, 1915, he awoke one morning with a peculiar sensation of numbness in the right shoulder. This persisted, and ten days later he noticed that the muscles of the right shoulder seemed to be getting smaller. In September, 1915, the muscles of the left shoulder began to "shrink up," but this atrophy was not accompanied by any sensory disturbance. The atrophies in the two shoulders and arms have been gradually progressive. At various times, especially after exertion, he has noticed twitchings in the muscles of the hands, back, and arms.

In his previous history there is the chancre in 1894, pneumonia in 1891, repeated attacks of malaria—he was a soldier in the Philippines—and gonorrhea in 1907. He drank excessively, four or five glasses of beer daily and ten to twenty-five glasses of whisky a day; he also smoked twenty cigarettes daily. There

has at no time been a history of pain in the shoulders or arms. In 1907 he suffered an attack of severe pain in the knee, shin, and foot of the left side. At this time he was in Cuba. One morning the anterior portion of the foot became "black." The doctor made a crossed incision, the scar of which is still visible on the dorsum of the great toe. There was a profuse, dark bloody discharge which lasted for about twenty days. The cause of this attack is unknown; it may have been some vascular disease peculiar to the tropics. At any rate, we cannot with safety assume that it was a symptom of syphilis. The absence of pain or of any severe subjective disturbance previous to the onset of the present trouble is to be borne in mind.

Examination reveals, first of all, an inequality of the pupils. In a bright light the left pupil is considerably smaller than the right. When the light is shut out the pupils are approximately equal. There is no reaction to light in the right pupil; in the left the reaction, though of fair excursion, is sluggish; that is, the contraction takes considerable time for completion. Both pupils react fairly well to accommodation.

The cranial nerves are all normal except as shown by the fact that the left sternocleidomastoid muscle is considerably smaller than the right.

The upper group of erector spinæ muscles, those extending from the occiput to the atlas and axis, and those filling in the posterior triangles of the neck, are almost completely destroyed. This destruction is a little more marked on the right side than on the left; at least the hollow on the right appears a little more extensive than on the left, as you can very readily observe. The cervical as well as the scapular portion of the trapezius is entirely gone (Fig. 50). A few fibers of the acromial portion persist on the right side. The supraspinatus and infraspinatus show a tremendous atrophy on the right side, scarcely any fibers persisting. The atrophy is a little less marked on the left, where the supraspinatus fills up the mesial or spinal end of the supraspinal groove fairly well. The deltoids are completely destroyed on either side. The left biceps is also lacking; the right is represented by a cord about the thickness of one's index-finger (Fig. 50). The

triceps on either side is fairly well retained. The flexor groups of the forearms still persist; the right are better than the left. The extensors show marked atrophy. Pronation, accomplished with the aid of the triceps straightening the arm and the ulnar flexors

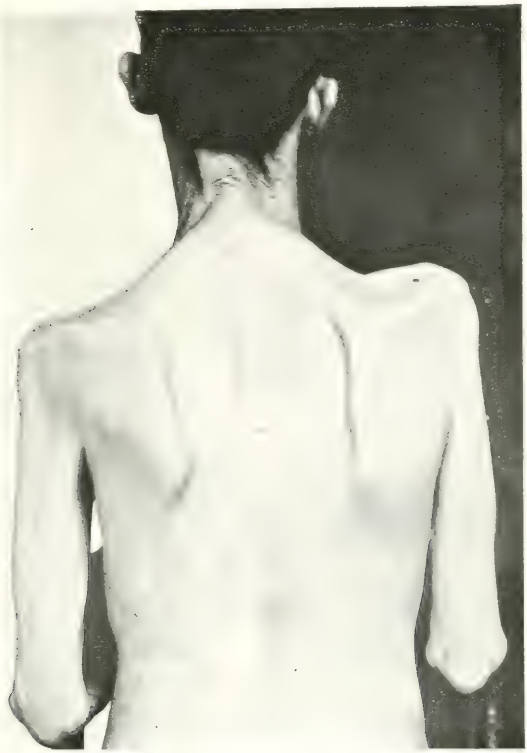

Fig. 50.—Shows extreme atrophy of muscles of the posterior cervical triangles; marked atrophy of the right supraspinatus and fair preservation of the left; atrophy of both infraspinati, right more than left atrophy of rhomboids with prominence of the spinous borders of the scapulæ; atrophy of the left latissimus dorsi with prominence of the lower angle of the left scapula.

bending the hands downward, is quite strong on the right, rather weak on the left. Supination is impossible. The pectorals are fairly well preserved, on the left better than on the right. There is a marked winging of the left scapula, very little of the right. The rhomboidei on both sides are entirely destroyed, as is shown

by the fact that when the arms are passively abducted there is no apparent muscular connection between the spinous border of the scapula and the bony spine (Fig. 51). The teres group on the right side is well preserved; on the left side it is almost gone.

In the hands there is a moderate degree of atrophy in the interosseous spaces and a rather higher degree of atrophy of the thenar and hypothenar eminences (Fig. 52).

Fig. 51.—Shows the atrophy around the shoulder-joint and of the upper arm.

These atrophies bring about the following anomalies of movement: Although he can turn the chin over either shoulder, and can hold the head erect so long as he stands erect, the minute he leans forward, so that the head is in front of the center of gravity, the muscles of the back of the neck, failing to act, allow the head

to drop forward. When he wishes to raise the head after it has dropped forward he has to do it by snapping it back with a rapid extension of the trunk from a bending to an upright position. He shrugs the shoulders by using the upper portion of the pectoralis major. The right shoulder moves higher than the left, this apparently being due in part to the few fibers remaining of the acromial portion of the trapezius.

Both the pectorals and teres major and minor cause this shrugging by forcing an approximation or narrowing of the shoulders

Fig. 52.—Shows the flattening of the thenar eminences on both sides. Both hypothenar eminences are also atrophic, but the picture makes only that of the left apparent

around the axis, so to speak, of the clavicles. The clavicles are fixed in their proximal and distal attachments. The pectoral group pull the upper end of the humerus inward. The only way in which this pulling inward can escape—that is, manifest itself—is by a lifting or pushing up of the outer end of the clavicle. The erector spinæ group of the upper part of the thorax is also atrophic. In the lower end of the thorax and in the lumbar region it is fairly well preserved.

The right latissimus dorsi shows a fair degree of function, so that the right scapula is held against the side of the chest at its lower angle. The left latissimus dorsi is entirely atrophied, the lower angle of the left scapula standing out boldly from the side of the thoracic wall. The left supraspinatus is felt in the supraspinal groove. When the patient attempts to cross the left arm in front of the chest the supraspinatus is felt to contract strongly. This crossing of the chest is impossible with the right arm; the right supraspinatus is completely atrophied. The right serratus magnus is fairly well preserved; the left is incapable of any degree of function. This is shown by the fact that the right scapula maintains its position close to the chest wall as the patient attempts to push straight ahead of him with the outstretched arm, whereas when this movement is attempted with the left arm the scapula stands out from the chest, rotates, its lower angle moving inward and upward, and the pushing movement is much feebler than on the right side.

The patient is entirely unable to abduct the arms; they hang at his sides without the slightest movement, owing to atrophy of the deltoids and supraspinati. He is unable to flex the left elbow, but has fair power of extension. He has a fair grip in the left hand with good ulnar flexion. Extension and radial flexion are abolished. He can approximate the thumb to the tip of the first and second fingers, but not to the last two. As I said previously, pronation is possible, but not supination.

In the right arm there is a fair degree of flexion of the elbow through use of the biceps; the supinator longus is destroyed. Extension at the elbow is better than it is on the left. The same anomalies of movement exist in the wrist, hand, and fingers as on the left side. The muscles of the lower extremities are well preserved.

A careful examination of the *sensorium* reveals a narrow strip of hypalgesia and hypesthesia about 1 inch in width over the third right interspace. Pain, both deep and superficial, is slightly diminished in the lower legs. There is a slight increase of swaying as he stands with closed eyes in the Romberg test. The reaction of degeneration is present in most of the muscles of

the shoulder girdle, the left biceps, and the extensor groups of the forearm.

Lumbar puncture on May 9th revealed 12 cells to the c.mm. and the Nonne test was positive. On May 20th there were 10 cells to the c.mm. and the Nonne again was positive. The Wassermann tests on the spinal fluid were both negative. The urine was normal and an *x*-ray picture of the spine in the upper cervical region showed no abnormality.

The *reflexes* are as follows: The plantar reflexes on both sides are normal; the Achilles are slightly reduced, though nothing abnormal is demonstrable. The same is true of the patellars. The cremasterics are barely demonstrable. The abdominal reflexes are normal. The wrist-jerks are lost, as are the biceps; the triceps jerks are preserved. The jaw jerks are lost.

Differential Diagnosis.—The diagnosis of this condition lies between progressive muscular atrophy of an idiopathic nature, such as was first described by Charcot, syringomyelia, myopathy; that is, a progressive muscular atrophy due to changes in the muscles themselves and progressive muscular atrophy of a symptomatic nature; that is, due to some underlying disease of the spinal cord.

The progressive muscular atrophy of Charcot rarely shows the tendency to pick and choose muscular groups evident in this case. It is rare also for it to involve the muscles of the posterior cervical triangle. Then, also, to eliminate the progressive muscular atrophy of Charcot, or the idiopathic form, we have evidence of other involvement of the nervous system, as manifested by the pupillary inequality with the failure of reaction to light and preservation of reaction to convergence in the right pupil. Also in the idiopathic variety sensory changes are unknown. In this case there is an involvement in the thoracic region and in the lower legs.

Syringomyelia practically always comes on in the second or third decade of life. In syringomyelia, as you know, the sensory changes are very marked and are found most frequently in the regions where the muscular atrophies occur. Sensation in this man's arms, shoulders, and chest, with the exception above men-

tioned, is normal. The disturbance of sensation in this case, involving the lower legs and a band around the thorax, is that most frequently seen in nervous syphilis. Syringomyelia usually shows some bony changes where the muscles of the trunk are markedly involved. If this man's atrophies were due to syringomyelia we might expect a scoliosis or kyphosis.

In myopathic progressive muscular atrophies showing no change in the central nervous system, but proceeding directly from the muscles themselves, a distribution of atrophies similar to that seen in this man is not infrequent; that is, a preponderance of the atrophy about the proximal portions of the limbs and about the shoulder girdle. But we do not find relatively normal muscles in the midst of highly atrophic muscles, as, for instance, the left supraspinatus and the right teres group spared in this case. Weakness and atrophies of the erector spinæ muscles are very common in the myopathies, but they usually attack the erector spinæ muscles in the lumbar region. The myopathies also practically always begin before the age of twenty. This man was a soldier in the United States Army up to ten years ago. Naturally, any degree of muscular weakness would have disqualified him long before that. Reaction of degeneration is not found in the myopathies. Neither are the pupillary nor sensory changes found in this patient. Fibrillary twitching is not seen in the myopathies.

Progressive muscular atrophy has been ascribed to tuberculosis. You all know of the atrophies seen around a tubercular joint. They are unquestionably due not only to disuse, but also to nerve influence. After this patient had been in the hospital a few days an evening rise of temperature of 1 to 1½ degrees was observed. Difficulty in breathing was complained of, a pulse running from 85 to 120 was recorded, and fluid was demonstrated in the left thoracic cavity. A small amount was aspirated, but the pneumococcus was discovered. At the apices of both lungs there was dulness, tubular breathing, and fine, crackling râles could be heard. In other words, the man probably has an inflammatory pulmonary disease, very probably of a tuberculous nature. Such a wide-spread muscular atrophy due to tuberculosis has never

been described. I consider the tuberculosis as merely concomitant.

We have, however, a history of a chancre in 1894, insufficient treatment, and the use of alcohol. Extensive muscular atrophy of the kind seen in this patient has been described in patients clearly showing other evidences of syphilis who at postmortem have been proved to have syphilis. The evidences in this man are fairly strong that syphilis is the cause of his trouble. The history, as I have mentioned, the pupillary anomalies, inequality, failure of reaction to light in the right pupil, sluggishness in the left, and the sensory disturbance around the chest and on the lower legs. The spinal fluid, showing as it does an increase in the cell content, merely shows organic disease of the central nervous system. The Wassermann is negative. A negative Wassermann is frequently met in a case of this sort where the disease is parenchymatous, and where from the symptoms it is reasonable to suppose that only a small amount of nervous tissue is undergoing syphilitic invasion. That is, parenchymatous syphilis, such as paresis, practically always gives a positive Wassermann, but in a case of paresis there is also involvement of the meninges and the parenchymatous invasion is very extensive, involving as it does a large portion of the cerebral cortex. In this patient we can assume an involvement of only about 4 or 5 inches of the anterior horns of the spinal cord.

So, in spite of the negative Wassermann, I feel that we are justified in ascribing this muscular atrophy to syphilis.

Treatment, unfortunately, would do very little in this case other than stop the further progress of the disease. He is, however, having mercurial inunctions twice daily. For the first week they were 1½ drams per inunction, but at the end of five days a slight amount of salivation developed, and the dose was reduced from 3 drams daily to 2 drams daily.

A CASE OF BEGINNING GENERAL PARESIS

I WANT now to show you another case of a parenchymatous syphilis in which there is a strongly positive Wassermann reaction.

This man is a printer, single, forty-six years of age. He came into the hospital on the 14th of June complaining of clumsiness and weakness in the right hand and leg, pain in the abdomen, difficulty in walking in the dark, and involuntary urination. The fact that he is a printer, handles type, and, therefore, is subject to lead-poisoning, complicates the diagnosis to a certain degree. Two years ago he noticed that he could not pick up the type as well as usual with his right hand. In fact, he was forced to quit his job. About a year later he noticed that his right leg dragged somewhat as he walked. For the past two years he has occasionally lost his urine at night, and of late he occasionally loses it in the daytime. For the past two months he has had considerable pain in the epigastrium, lasting practically all day. This pain, he says, is somewhat cramp-like.

In his past history there was a chancre twenty years ago and gonorrhea twenty-five years ago. The family history is negative. He drank from ten to twelve whiskies a day.

Examination reveals irregularity of the pupils, the right being larger than the left; they both react well to accommodation, but not to light. His teeth are in frightful condition; the gums are swollen, and along the edge bordering the carious teeth there is a discoloration which suggests the blue line of lead-poisoning. The heart is normal. There is an inequality of facial response; the right facial reacts to volition and emotion better than the left. There is a right hemiplegia of slight degree, the right foot drags and sticks to the floor. He is able to maintain his left arm in a fixed position, resisting the efforts of the examiner, better than he can his right. There is very little, if any, difficulty shown in the ordinary finger-to-nose and heel-to-knee tests. All the deep

reflexes are exaggerated. There is a slight knee clonus in the right leg and the right plantar reflex is not as frank as the left. There is a bilateral Chaddock sign, more marked on the right than on the left. The sign has much the same significance as the Babinski sign. It is brought out by scratching the patient just below the external malleolus. As we perform the test on this man you see that there is not only a slight fanning of the toes—they spread apart—but also a definite dorsal flexion. There is a loss of pain sense in the lower legs, though the Achilles sense, the deep pain sense, is fairly well preserved. I can squeeze the left testicle with a great deal of force before he complains of pain. At times it seems as though the whole left side of the body felt pain less than the right. There is considerable slurring of speech, and he shows the following peculiar reaction to mathematic tests. I might say, in preface, that he has a high-school education.

$9\times7=72$; $4\times5=20$; $6\times5=30$; $9\times6=54$; $7\times8=56$; $9\times7=72$; $7\times8=56$; $9\times7=72$; $7\times8=56$; $7\times9=72$; $8\times7=56$; $9\times7=72$; $56+7=63$; $7\times9=72$; $8\times7=56$; $9\times7=72$; that is, though you see he is able to work out his multiplication fairly well up to 8×7, and when he adds 7 to that he is still correct, still the fact that he said $9\times7=72$ in the first place sticks in his mind with a peculiar tenacity. He seems to be unable to appreciate his mistakes.

Dr. Hamill (to Patient): If you went into a hat store to buy a hat for $2.75 and gave the clerk a ten dollar bill, how much change would you expect?

Patient: $7.25.

Dr. Hamill: If the hat cost $2.37, how much change would you receive from the ten dollar bill?

(Patient is utterly unable to work out the answer.)

He sits by his bed in the ward seldom speaking, showing very little interest in what is going on about him; he strikes one as being very apathetic.

The laboratory tests show a normal urine; the spinal fluid shows 18 cells to the c.mm., with a positive Nonne reaction, increased globulin content. The Wassermann reaction on the blood was double positive; on the spinal fluid, triple positive.

The apathy and the poor showing in the mathematic tests suggest a diffuse cerebral involvement. The combination of paresis of the left facial with motor weakness and increased reflexes in the right arm and leg and sensory disturbance of the left side of the body indicate a lesion in the pons. Syphilis is the disease which most frequently causes such a multiplicity of lesions.

In considering the etiology of this condition we have to think of syphilis, alcohol, and lead.

He is a printer, handling type. To support the diagnosis of lead-poisoning is the gastric distress of a cramp-like nature, the evident anemia which you see, and the suggestion of a lead-line in the gums. There is, however, no particular preponderance of weakness in the extensors of the wrist, such as we see in lead paralysis. Rather, this man is weak all over, and has a slight hemiplegia of a pontine type.

I neglected to state, in speaking of the laboratory findings, that examination of the blood revealed a simple anemia, but no degeneration of the red cells, such as is seen in lead-poisoning.

Alcohol can be eliminated as the essential etiologic factor in the same way as lead so far as symptoms are concerned; that is, alcohol, though producing the tremor seen in this man and the mental stupidity, shows itself most frequently in a symmetric paralysis involving the extensors of the lower legs and the feet, and not showing a hemiplegia, such as is present in this man.

The pupils, the tremor about the mouth, the mental difficulty, and the hemiplegia all belong to the picture of beginning paresis. This is borne out by the spinal fluid and blood tests.

Although we must consider syphilis the essential cause of this patient's disease, still both lead and alcohol are known to be causes of diseases of the nervous system; they should be considered as contributory factors.

This man's mouth is in such a frightful condition that mercury is contra-indicated. It would be impossible to give him enough mercury to saturate him with this salivation already existing. Arsenic, then, is the drug of choice in his case. Recent reports of the use of arsenobenzol would lead me to recommend it in this case. I should give it in 2-, 3-, or 4-decigram doses at three- or

four-day intervals. He should have at least fifteen such treatments. The medicine must be given intravenously, great care being taken not to allow any of the solution to escape either into the wall of the vein or into the tissues surrounding the vein.

The teeth and gums must be put in good condition, precautions must be taken to avoid further poisoning from lead, and alcohol is to be strictly prohibited.

CLINIC OF DR. FREDERICK TICE

COOK COUNTY HOSPITAL

CARCINOMA OF THE HEAD OF THE PANCREAS

Differential Diagnosis of Tumors in the Region of the Gall-bladder Associated with Jaundice. Typical Sequence of Symptoms Pointing to Carcinoma of the Head of the Pancreas: (1) Gastric Disturbance; (2) Progressive Jaundice; (3) Tumor Mass Near Location of Head of Pancreas Associated with a Distended Gall-bladder.

May 8, 1916.

THIS patient presents an interesting condition, particularly in association with the recent case or two of cutaneous pigmentation. She has a universal jaundice, definite and distinct. Not only the external surface of the body but also the mucous membranes and conjunctiva are affected. The mucous membranes of the mouth and under surface of the tongue are all decidedly pigmented.

Present History.—The patient is fifty-five years old, and entered the hospital on May 1st with a diagnosis of Addison's disease and nephroptosis. She complains of vomiting, pigmentation of the sclera, and loss of weight. She has always been strong and healthy up to eight months ago, when she began to have nausea and spells of vomiting, usually occurring in the evening or at night, never immediately following eating. The vomiting was not associated with pain or headache, but considerable belching occurred. The vomitus consisted of greenish-yellow material, never of food particles or blood. Her appetite remained good. A period of constipation usually preceded each of these attacks. The vomiting lasted for a couple of days and made

the patient quite weak; the attacks occurred at intervals of one to two weeks. After meals there was often a feeling of weight in the epigastrium, but no real pain. The discoloration of the sclera was first noticed two months ago, six months after the onset of the trouble. Since then it has varied slightly in degree, increasing gradually, particularly at the time of her attacks of vomiting. She has noticed a loss in weight of 15 pounds during the last three months. This is associated with a general weakness. There has been no cough, no dyspnea, no edema at any time; no renal disturbance, except occasional nocturnal urination. The bowels are usually slightly constipated; there have been no chills and no fever.

Past history is negative; she has had no illness of any kind.

Family history is also negative; she has two children living and well and there is no history of miscarriages. Venereal infection is denied and there is no history of the use of alcohol.

Laboratory Findings.—An Ewald test-meal was given on May 3d, and in one hour 30 c.c. were removed. Examination showed 10 degrees free hydrochloric, total acidity of 40 degrees, a small amount of mucus, and no blood. A motor-meal was given, and at the end of six hours 30 c.c. were recovered. No recognizable residue was present.

Feces Examination.—The amount was large and clay colored; no mucus, no pus, no blood by the Weber test, and no bile was found.

Urinalysis.—The specific gravity varied from 1008 to 1015, reaction acid, no albumin, no sugar, but a large amount of bile was present.

Blood Examination.—The hemoglobin was 45 per cent., the red blood count 3,280,000, and the whites 9000; there was a slight increase in the polymorphonuclears; otherwise the differential count was normal.

Physical Findings.—The first examination of this patient a few days ago was unsatisfactory, as the abdomen was so distended and tympanitic that it was impossible. Since then she was given a cathartic and a colonic flushing last night and again this morning, with the result that a very definite tumor mass can be

felt in the right hypochondrium. Perhaps we would better indicate three tumor masses—one extending down practically to the crest of the ilium.

On inspection of the abdomen, aside from the jaundice, there is nothing that particularly attracts the attention. There is perhaps some increase in the pulsation, but there is no bulging tumor mass. On palpation, however, you at once encounter on the right side of the abdomen a mass extending down to the crest of the ilium. This is rather globular, smooth, and freely movable. By pressure in the lumbar region it can be displaced anteriorly, and pressure from the side produces a bulging. We also find it descends a little with respiration. To the inner side we encounter another mass, with a groove separating the two, and the second mass is also globular. Just above the umbilicus there is a third mass which is definitely tender, only a slight amount of pressure producing discomfort. Unlike the other two masses, this is irregular, nodular, and not movable. Either of the tumor masses to the right of the median line descends very well with respiration and is quite freely movable upon palpation. The central mass moves only slightly with respiration and it is impossible to move it by pressure.

Röntgen Findings.—The patient received a barium meal early in the morning and at the end of six hours was fluroscoped. The following report by Dr. Blaine was made: A small six-hour residue is noted. The stomach empties within a few minutes. Very active, deep peristalsis is present. No defect in the stomach outline is seen. The duodenal bulb is complete. The stomach is low down in the pelvis and unusually long.

DR. TICE: Now, what is your opinion?

DOCTOR: I think there is a malignancy.

DR. TICE: There is the history of an illness of eight months' duration, the gradual loss of weight, a jaundice which has existed for two months, gradually increasing in intensity, the presence of a mass in the abdomen, and it is fairly safe to conclude there is a malignancy. Where is this tumor located?

DOCTOR: From the history and the location of the tumor mass I believe there is a gastric carcinoma.

DR. TICE: Where else might the tumor originate?

DOCTOR: It might be in the duodenum. It is not at all uncommon, but not as frequent as a gastric carcinoma. It might be a cholelithiasis.

DR. TICE: What else might you think of?

DOCTOR: Carcinoma of the gall-bladder.

DR. TICE: We have here three definite, distinct tumor masses, one of which may be the gall-bladder. It would seem, so far as we can determine from our physical examination, and also from inflating the colon, that the mass to the right is a movable kidney. The second mass gives the impression of a distended gall-bladder, but what is the mass that is tender, the one in the median line, the one that is nodular, fixed, that does not move upon pressure or upon respiration? Is that a duodenal carcinoma, a gastric carcinoma, or what is it?

DOCTOR: It might be the transverse colon.

DR. TICE: Hardly; a tumor of the transverse colon is usually freely movable. What about a carcinoma of the head of the pancreas? That is a possibility, and some of the clinical considerations, particularly from the standpoint of differentiation, we will consider at the next hour.

May 15, 1916.

DR. TICE: You will recall the patient presented in the clinic a week ago, the woman with the intense jaundice. You will remember that there were physical signs of some abdominal involvement, with a tumor mass in the right hypochondrium, another approximately in the region of the gall-bladder, and a third mass more nearly in the median line. At that time we did not discuss the possibilities, but were all impressed with the probability—considering the woman's age, the duration of her illness, the jaundice, the loss of weight, and the presence of the abdominal tumors—that she had some sort of a malignancy. A provisional diagnosis was made of a gastric carcinoma. She had, as you will recall, some gastric disturbance, nausea, and vomiting, but the test-meals showed a normal acidity and no blood was present. A motor-meal was also negative, as well as the fluoroscopic and *x*-ray examination.

One stool examination was reported at that time, and two subsequent examinations have been made with an absence of blood, so it seems reasonable to exclude the existence of a gastric carcinoma.

Differential Diagnosis.—The presence of the jaundice, which has existed over a number of weeks and has become more and more intense, brings up a consideration of the causes producing an obstruction of the biliary tracts. A cholelithiasis was mentioned as a possibility, but this patient at no time has suffered from any distress which might be interpreted as a gall-stone colic. There is no history of previous attacks of jaundice. While it is perfectly possible to have a cholelithiasis and a stone in the common duct producing obstruction without definite colic, nevertheless we lay particular stress in the diagnosis of cholelithiasis on attacks of colic. Attacks of colic even without jaundice are definitely in favor of gall-stones.

A diagnosis of carcinoma of the gall-bladder was suggested, or perhaps better, a carcinoma of the gall tracts, either involving the gall-bladder itself, or the cystic duct, or the common duct, particularly in view of the fact that a tumor was present in the region of the gall-bladder and another near the median line.

The diagnosis of carcinoma of the gall-bladder or gall tracts is usually made from a clinical history of previous attacks of gall-stone colic, with the subsequent development of a tumor, particularly a nodular tumor, in the region of the gall-bladder. In the absence of gall-stone colic a diagnosis of carcinoma of the gall-bladder is difficult, and it is usually recognized only at the time of an exploratory laparotomy. Even at that time, and without the assistance of microscopic examination, a diagnosis of carcinoma is not always possible. We can recall one patient operated not long since with an intense jaundice, in whom the walls of the gall-bladder were found enormously thickened, and a diagnosis of carcinoma was made; the gall-bladder was not removed, but simply drained. The jaundice promptly disappeared and a carcinoma was evidently not present.

If a patient gives a history of recurring attacks of gall-stone colic and then develops a tumor, particularly a nodular tumor,

associated with increase in the jaundice and loss of weight—especially after fifty years of age—a diagnosis may be made of carcinoma. In the absence of the colic, even in the presence of a loss in weight, the diagnosis can only be speculative.

A carcinoma located in some other portion of the biliary tract was a possibility in this patient. In this connection it is necessary to mention that the carcinoma may be in one of several locations to produce an obstruction. The carcinoma may involve the common duct, produce an obstruction, and the jaundice become progressive in type. That is one of the distinguishing features of a carcinoma in this location—that the jaundice is progressive. Clinically, there is little or no disturbance of the pancreatic function, for the reason that the pancreatic duct is not involved or compressed beyond the location of the primary involvement. Subsequently, as the tumor becomes larger, there may be a compression of the pancreatic duct.

A carcinoma may involve the pancreatic duct with disturbance of the pancreatic function, but without the production of a jaundice, for the reason that the biliary tract is not involved. Or an involvement of the diverticulum may occur, and when this happens not only does the jaundice become more and more intense, because of the complete cutting off of the biliary tract, but there is also an associated pancreatic disturbance and not infrequently a resulting fat necrosis.

The most frequent location of a malignancy involving these tracts is within or below the common bile-duct, most frequently involving the epithelium of the papilla. This usually is manifest by the development of jaundice which is intermittent in character, for the reason that the tumor mass usually makes a varying degree of pressure, either because of the location of the tumor or because of its destructive process.

Then quite frequently, in association with a carcinoma of the papilla, blood is present in the stools from time to time, but not constantly.

Another location for a carcinoma, and one producing, as a rule, a progressive type of jaundice, is in the pancreas and, for practical purposes, the head of the pancreas. A carcinoma of the

tail or body of the pancreas is not associated with jaundice unless metastases occur. But a carcinoma of the head of the pancreas can and does produce a jaundice, either from involvement of the biliary tracts or from metastases. Clinically, a carcinoma of the head of the pancreas is indicated first by gastric disturbance, interference with digestion, distress after eating, and subsequently nausea and vomiting. A second group of symptoms result from compression or pressure of the tumor. Of these, perhaps of the greatest importance is the jaundice, from the compression of the duct either directly by the tumor or by metastases. Pain is quite constantly present, usually sharp in character, and often accompanied by pain or distress in the back. A rapid loss of weight is another symptom, perhaps with a glycosuria, and with an increased volume of the stools. Patients will frequently remark that there is an increase in the amount of feces in proportion to the amount of food consumed. Another finding is an increase in the fat content of the stool.

Examination of the feces in the patient presented reveals a definite increase in the amount of fat in the stools.

A third stage in pancreatic carcinoma consists in the presence of a tumor, usually located in the epigastrium, more or less fixed, and perhaps nodular in character.

The symptoms and physical signs in the patient presented would justify a clinical diagnosis of carcinoma of the head of the pancreas on the basis of, first, the gastric disturbance; second, the appearance of the jaundice, progressive in type, becoming more and more intense; third, the tumor mass at or near the location of the head of the pancreas, nodular in type, rather fixed, and associated with a second tumor mass which we interpret as a distended gall-bladder.

At this time reference should be made to Courvoisier's law, which has to do with a differential diagnosis of a cholelithiasis and a carcinoma in the presence of jaundice. It is quite generally accepted that a jaundice associated with a large, palpable gall-bladder indicates malignancy; unassociated with a palpable gall-bladder indicates a cholelithiasis.

In this patient the gall-bladder is large, palpable, distended,

and smooth. This is another confirmatory sign of a pancreatic carcinoma. The existence of the jaundice and the presence of a large, palpable gall-bladder is frequently referred to as the Bard-Pic syndrome.

The third tumor mass was interpreted as a movable, palpable kidney, moving freely with respiration, with a kidney ballottement.

The clinical course has not changed materially since a week ago. As far as the **treatment** is concerned, that is purely palliative. No surgical interference is indicated. The only possible excuse for surgical interference would be an exploratory laparotomy, which is hardly justified, for we feel reasonably sure that it is a pancreatic carcinoma and inoperable.

CHRONIC BRONCHITIS, EMPHYSEMA, AND MARKED CYANOSIS. CONSIDERATION OF CONGENITAL HEART LESIONS. OTHER CAUSES OF CYANOSIS.

April 17, 1916.

Present History.—This patient is thirty-three years old, and entered the hospital on April 5th with the following history: She was taken sick six days ago, but remained at work on that day. The next day she was confined to bed. Previous to this she was fairly well and at work in a packing-house in the stockyards. The present complaint consists of a cough and expectoration of a large quantity of mucopurulent sputum. She is short of breath, weak, and has had some pain in the substernal region of the chest.

Previous History.—The patient has never been strong, but has never suffered from any serious illness. She thinks she has always been short of breath and has had a cough continuously, but this has not incapacitated her. During the present illness there have been no chills or vomiting, no fever, and no pain except as above noted. The bowels are usually constipated. The patient has noticed no change in the frequency or amount of urine. She does not use alcohol, has never been married, and denies venereal infection. Her menstrual periods began at the age of thirteen. She was always irregular, and about eighteen months ago there was a period of amenorrhea for six months. Since then the periods have reappeared and occur every four to six weeks. The amount of flow is small.

The *temperature* is recorded as 98°, 98.6°, or 99° F., and once reached 100.6° F. This slight elevation occurs in the afternoon. The pulse is recorded between 80 and 90, respirations 16 to 20.

Urinalysis is negative.

Physical Examination.—On first glance, in the general inspection of this patient, one is struck particularly with the degree of cyanosis. She is in the recumbent position and has not been

exercising; still, the cyanosis is very marked. The skin of the face, the lips, and gums is dark purple. The ears and the finger-nails are cyanotic; there is also a definite clubbing of the distal end of the fingers, the so-called Hippocratic fingers. The cyanotic condition is also present in the lower extremities, and you can observe the curving of the nails and clubbing of the toes, which is most marked in the great toes.

It is not definitely known why cyanosis occurs. There are several explanations and theories, but no one particular theory has been accepted. Clinically, cyanosis is associated with various conditions involving the pulmonary tract, the cardiovascular system, various blood conditions, or with some of the nervous diseases. The one condition in which the patient is relatively comfortable in spite of an extreme amount of cyanosis is an emphysema of the hypertrophic form.

Cyanosis is also associated with cardiac involvement, more particularly the congenital heart lesions. In the newborn the condition is known as "blue baby."

A relatively high-grade cyanosis results from the effects of certain drugs, the coal-tar group particularly. The administration of acetanilid, antipyrin, and the other coal-tar products will produce a high-grade cyanosis.

In this patient we have inquired particularly as to the onset of this cyanosis. She informs us that she has suffered from time to time with distress or perhaps pain in the substernal region, and that this condition has extended over a period of a number of years. At various times the condition has become so pronounced as to necessitate the application of counterirritation in the form of leeches. They have been applied at various times over the thoracic region and also over the sternal region, as you may observe by the numerous scars. At no time, however, has the disturbance been so acute as to incapacitate her or compel her to go to bed. She has been able to work most of the time, and only recently has the condition become severe enough to interfere with her labors in the packing department at the stockyards.

Assuming that this patient has had this difficulty from childhood or from early life, what evidence have we that she has a

congenital heart lesion? The cyanosis becomes more pronounced upon exercise and is accompanied with shortness of breath. Most of the patients with congenital heart lesions have dyspnea and we usually find clubbing of the fingers and toes. We also generally find in these cases an increase in the red cell count. One blood examination made on April 6th, an average of two different dilutions, revealed the presence of 6,400,000 reds, a white count of 9000, and hemoglobin 100 per cent.

Examination of the Heart.—On inspection the apex-beat is observed in the fifth intercostal space, in the normal location. There is no abnormal pulsation over the base of the heart and none in the vessels of the neck. The peripheral veins are perhaps slightly engorged.

On palpation we locate the apex-beat in the fifth interspace, which confirms the location on inspection. The beat is rather strong, circumscribed, unaccompanied by a thrill. There is no thrill over the base of the heart, but a rather distinct epigastric pulsation. The right border of the heart extends one finger-breadth to the right of the right border of the sternum in the fourth and fifth intercostal spaces. The base is at the lower border of the third rib. The left border is approximately in the mid-clavicular line. Over the base of the heart the area of aortic dulness is slightly increased.

On auscultation the tones at the apex are perfectly clear. No murmur can be heard and there are no murmurs over the body of the heart. In the left second intercostal space a very faint systolic murmur is present. Over the tricuspid area there is a systolic murmur; a murmur that is relatively as loud or slightly louder than the murmur in the pulmonary area. Both of these murmurs, however, are very faint and might be easily overlooked.

The congenital lesion most frequently associated with cyanosis, perhaps the most frequently encountered clinically, especially in adults, is pulmonary stenosis. This is a stenotic condition in the pulmonary area interfering with the flow of blood from the right ventricle into the lungs. It is recognized not only by the history of cyanosis and cardiac disturbance dating from childhood, but by the presence of physical signs, consisting of a thrill

in the pulmonary area, a murmur heard with the maximum intensity in the same area and transmitted into the pulmonary area and not up into the neck in the direction of the carotids.

On percussion the right side of the heart is found enlarged because of the dilatation and hypertrophy secondary to the pulmonary obstruction. These signs of pulmonary stenosis are not present in this case; we have no thrill, there is no murmur of any consequence in the pulmonary area, and no increase in the size of the right heart that cannot be accounted for on other grounds.

Another congenital lesion is due to a persistence of the communication between the auricles, consisting of a patent foramen ovale. Anatomically, this is not infrequent, but does not necessarily produce symptoms or signs. It rarely does so unless there is some other involvement of the heart disturbing the normal cardiac pressure. If a mitral incompetency results there may be an escape of the blood from the left into the right auricle, and this results in a cyanosis. In this condition there is usually to be heard a systolic murmur due to the escape of blood through the patent foramen.

Another congenital condition is a patent ductus arteriosus. This produces cyanosis, and physically the findings consist of a murmur which is systolic-diastolic. There is a continuous hum, perhaps varying in intensity with systole and diastole. No such condition is present here.

So it would seem improbable to attempt to account for the cyanosis on account of a congenital heart lesion. The cyanosis has existed for a number of years, but the physical signs are not indicative of a congenital heart deformity.

A cyanosis associated with an acquired heart lesion is rarely found except in the last stages of a broken compensation. Then the degree of cyanosis is much greater than that which is present here, and is almost invariable associated with dyspnea. This patient would be up and about if we would allow her to be. Yesterday she insisted upon having her discharge, maintaining that she was able to go back to work.

The Examination of the Lungs.—Upon inspection we find no

marked difference between the two sides of the chest. There is perhaps a tendency toward an increase in the anteroposterior diameter. On percussion there is a hyperresonant note and an increase in the extent of the resonance downward. It extends one intercostal space lower than normal. Posteriorly the lower border extends low on either side, but it is impossible to determine the amount of the respiratory excursion, for the reason that the patient does not speak English. On auscultation the breath sounds are relatively rough. Perhaps the expiration is a little prolonged, while inspiration is accompanied over all portions of the chest with a large number of wheezing râles. The auscultatory findings rather suggest the pulmonary findings which are obtained after the subsidence of an attack of bronchial asthma.

The Examination of the Abdomen.—The liver in the nipple line is felt two fingers below the costal border. The edge and surface of the liver on palpation are not rough, but smooth. The spleen extends one finger below the costal border. It is hard and smooth. There is no fluid in the abdomen and no edema.

So far as we can determine, this patient presents, aside from her cyanosis, the physical findings of a pulmonary involvement. There is no history that we can elicit that she has ever expectorated blood; there is no history of a tuberculosis; the temperature has not exceeded 100.6° F. The sputum examinations so far are negative for tubercle bacilli.

The x-Ray Examination.—The pulmonary shadows show a marked increase, the characteristics of which indicate a chronic bronchitis.

We can go no further than to make a clinical diagnosis of a bronchitis; the exact nature will have to be determined by the subsequent examination of the sputum, and this condition is associated with a moderate degree of emphysema. When this patient entered the hospital the physical examination revealed an enlarged liver and also an increased right heart. At that time the lower border of the liver was on a level with the umbilicus, slightly tender, but did not pulsate. According to the statement of the examining physician at the time she entered, this was somewhat greater than can be demonstrated at this time.

How can we explain these conditions? Perhaps on the basis of a bronchial involvement, a chronic type of bronchitis with recurring attacks existing over a long period of time, ultimately resulting in a moderate grade of emphysema, with an interference with the function of the right heart, with some dilatation, with a resulting engorgement of the liver, and also a slight enlargement of the spleen. The fact that the heart has decreased in size, that the liver is materially smaller and is no longer tender, would rather indicate some temporary involvement of the right heart. This we can easily account for on the basis of the emphysema for the reason that in an emphysema sooner or later the right heart becomes dilated, and perhaps a moderate amount of the cyanosis occurring in an emphysema is due not to the pulmonary involvement alone, but to the cardiac involvement as well.

The cyanosis in this patient may be accounted for on the basis of the bronchitis and emphysema and the recent temporary disturbance of the function of the right heart. While it is impossible to diagnose a congenital heart lesion, it is equally impossible to absolutely exclude it. In a patent foramen ovale, particularly in the newborn, cardiac signs may be entirely absent. Not long since repeated examinations of a "blue baby" in one of the private hospitals constantly failed to reveal any sign of a cardiac lesion. The baby lived only a few days, and the autopsy revealed an immense patent foramen ovale. While a congenital heart lesion cannot be excluded, one would be inclined to believe that if a congenital heart lesion was present and had existed over thirty-three years there would be some cardiac signs.

Another disease, erythremia or Vaquez's disease, characterized by a splenomegaly, an increase in the number of red cells, and a cyanosis, should be mentioned. As a possibility in this case it has not been seriously considered, as the increase in the red cells is more marked and the enlargement of the spleen more pronounced.

CLINIC OF DR. JOSEPH ZEISLER

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL.

ETIOLOGY AND TREATMENT OF ACNE

Clinical Varieties of Acne. Anatomic, Physiologic, and Microbic Factors in the Etiology. Practical Failure of Vaccine Therapy. Systemic and Local Treatment.

THE cases which are before you today present no diagnostic difficulties and are far from being medical curiosities. They, in fact, form the most common ailments of the skin which we are called upon to handle, and it is for this purpose especially that you should be thoroughly acquainted with their nature and management.

Acne has for a number of years occupied quite an important place in dermatologic practice on account of biologic studies concerning its cause and the treatment based upon its supposed etiology. But let us first analyze briefly the material at hand.

The first patient, a young man of eighteen, apparently healthy looking, with a rather dark, coarse skin, has been troubled for several years with the ailment for which he seeks relief. You find a great number of small brownish and almost black points or dots disseminated over his face, some upon his back, and particularly upon the inside of the ears. There seems to be no further inflammatory process present. This is the form of acne known as *acne punctata*, in which comedones are practically the only essential feature. These comedones or blackheads consist of inspissated sebum, plugging the excretory duct of the sebaceous glands. The dark color at the top is not, as popularly supposed, an ac-

cumulation of foreign material, but is due to a chemical color change, as first proved by Unna, who demonstrated the presence of a definite pigment called "ultramarine" in them.

Upon the back you will observe a peculiar variety of these comedones in the form of double, triple, or even quadruple comedones.

The removal of these blackheads is a comparatively easy matter by merely expressing them, but occasionally you will find them so deeply and firmly embedded in the skin that a small incision is necessary to evacuate them. Particularly is this the case in the ear, where the sebum is compacted at times in such large masses that their removal is not only painful to the patient, but quite laborious for the physician.

The next patient presents a somewhat more complicated picture. This young lady of twenty-three has been troubled for many years. We find her complexion rather greasy looking. She appears frail, somewhat pale, her hair is thin, her scalp is affected by dandruff, she complains of habitual constipation, menstrual irregularity, and frequent headaches. On her face you find not only a great many comedones, but a number of dry, reddish papules and pustules, a large number of superficial and more deeply seated cutaneous abscesses and nodules, and many scars, evidently the result of previous pustules. On her back and the upper part of her chest you observe many similar lesions. Here you have the typical picture of an ordinary acne, or so-called *pustular acne*.

The next case, a young man of twenty-six, shows his face rather free of any lesions, but upon his back, his chest, and his upper arms there are a large number of deep-seated, firm nodes and flabby cutaneous abscesses. This is the form usually known as *acne indurata*.

All these types belong to what is commonly known as *acne vulgaris*. It may not be amiss, however, to remind you that the term "acne" is frequently used in connection with various designating adjectives for other forms of skin diseases quite distinct from it. What is known as *acne rosacea* is a common disorder, occurring, however, principally in middle life, as differentiated

from the adolescent period of the former. It is chiefly due to circulatory disturbances of an angioneurotic character, with telangiectases, leading to a chronic passive hyperemia of the nose, chin, and forehead, and in its worst forms producing a hypertrophy of the tissues, a grotesque cauliflower enlargement of the nose, known as "rhinophyma."

Under the title *acne varioloformis*, or *acne necrotica*, is described a rather unusual eruption located chiefly on the forehead, the scalp, nose and cheeks, and occasionally on the back, beginning with firm, pale reddish papules, which become pustular and undergo central necrosis. Gradually they desiccate to firmly adhering crusts, which eventually drop off and leave conspicuous depressed scars not unlike those remaining after small-pox. We have good reasons for considering this form of acne as one of the varieties of the so-called "tuberculides."

Likewise must be classed under the same head another variety of acne known as *acne cachecticorum* or *scrofulosorum*. This is a more generalized eruption of foul-looking purplish pustules and nodules on the extremities and the trunk which occurs in tuberculous and anemic subjects.

What is known as *bromid acne* or *iodid acne* is an eruption of pustules and papules on the face and shoulders, which is the direct effect of the ingestion of these drugs, and is generally considered under the heading of *dermatitis medicamentosa*.

Etiology.—What interests us today in the cases of acne vulgaris which you have inspected is their cause and treatment. These also are the questions by which we are confronted daily by our patients at their first visit. The anxious mother wants to know what this eruption comes from, whether it is the blood or the diet or something else, and she wants to know whether it "can be cured to stay cured." The family physician has made light of it, promised that the child would outgrow it, but in the meantime the young lady is thoroughly miserable, feels herself socially ostracized on account of her condition, and considers the matter rather seriously.

A great many elements enter into the causation of acne. There is a structural or anatomic feature, there are pronounced

physiologic disturbances, and there is unquestionably a microbic factor.

The structure of the skin, the presence of an excessive sebaceous development, cannot be ignored. A coarse skin, one that is poor in elastic fibers, is manifestly more likely to be affected by acne than is a complexion delicate in character, light in color, rich in elastic elements.

To the microbic influence has been assigned, particularly in recent years, a very important rôle based upon the presence of supposedly pathogenic organisms. Years ago Unna succeeded in cultivating a peculiar microbacillus, and later Gilchrist insisted upon his bacillus acnes as the chief cause of the disease. Sabouraud described a microbacillus of seborrhea which he held to be the cause of the excessive secretion. There is no reason to doubt that these organisms as well as the ordinary staphylococcus are abundantly present in every case of acne, but a legitimate doubt may be entertained as to their essential causative rôle in the presence of other overwhelmingly important causative features. The outstanding fact must not be lost sight of that acne never occurs before puberty and has a natural tendency to disappear during married life. Its occurrence chiefly during adolescent age, therefore, must lead us to look upon physiologic and anatomic processes during that period as bearing upon the cause of the disease. The overactivity of the sebaceous and pilous system during this period is of paramount importance.

Why should specific micro-organisms be active during this period and not before, and not in later mature years? The answer we get to our question from the adherents of the microbic theory is evasive. They point to the parallel presented by ringworm, which occurs in young subjects, but disappears spontaneously after puberty.

No really unquestioned production of the disease by the pure cultures of the acne bacillus or other organisms has been demonstrated, and why should these organisms cease to be detrimental as soon as a young woman enters matrimonial life? Is it not much more plausible to look upon the generative organs, or rather disturbances in their physiologic action, as the chief un-

derlying element of acne? We are only at the threshhold of our knowledge of the rôle which the hormones, those secretions of the ductless glands, play in the human economy. In the first rank of these glands stand unquestionably the so-called gonads, or male and female sex glands, and their relation to the production of acne appeals to the unprejudiced mind as much more essential than any other factor. No doubt digestive disturbances are present in a majority of the cases, but these may be secondary to the other underlying cause.

Similarly, we know that many dietary articles are directly productive of acne lesions, the absorption of toxic products from the intestines probably acting as vascular irritants. Herein we can see a clear analogy to lesions resulting from the ingestion of iodids and bromids. But here, again, we are confronted by the fact that a good many individuals can tolerate any and all kinds of food without the slightest effect upon their skin, and that only those who have a predisposition toward acne exhibit marked sensitiveness.

With all admiration for the splendid and painstaking work in the direction of establishing the microbic origin of acne, I fear that most of that work will have only an academic character.

Vaccine Treatment.—This leads me to a phase of the treatment of the disease which in recent years has come to occupy the foreground of attention. I refer to the use of so-called vaccines. Employed first under the head of opsonin treatment, we have been using autogenous vaccines, both of the acne bacillus and of staphylococci, grown from the pus of the acne pustules of the patient, and later the so-called "stock" vaccines, not only of special organisms but also the so-called "mixed" vaccines, containing as nearly as possible all the different microbic elements found in the lesions of acne. These mixed vaccines, by the way, are one of the strongest arguments against the pathogenic rôle of any single organism, and contain an admission of uncertainty and weakness on the part of their advocates.

From a purely practical standpoint the use of vaccines in acne has been a decided failure. Reports of success in occasional cases have not been wanting. Permanency of results has rarely

been claimed and a majority of conservative practitioners have practically abandoned their use. If I mention in this connection the use of the so-called phylacogens which were urgently pressed upon our attention, I do so merely to condemn them in the treatment of acne from a few personal experiences which have taught me their harmful—at times almost alarmingly injurious—effect. If in treating a case of acne I should ever come to the point where I would be at my wit's end, I might think of the use of vaccines, but, fortunately, my experience has been that most cases respond readily to the management employed by me for many years.

Systemic Treatment.—The proper handling of a case of acne means a resourceful, comprehensive, individualizing employment of a great many therapeutic measures, both internal and local. The regulation of the diet, general hygiene, internal medicaments, local surgical and medicinal measures, and radiotherapy enter into it. I insist upon a carefully regulated diet, the chief features of which are simplicity, regular meal times, and thorough mastication. We know by experience that many articles of diet are almost directly responsible for the appearance of fresh lesions. Rich food in general, fatty gravies, spices, highly seasoned food, conserved meats and fish, highly flavored sauces, rich pastry, sweets, conserved fruits, fried food, cheese, condiments, alcoholics, and coffee are among the articles to be avoided.

A well-known Philadelphia dermatologist has recently proclaimed that his chief reliance in the treatment of acne patients is insistence upon thorough chewing of the food. Another dermatologist, in a recent discussion of the subject, places all the blame upon insufficient elimination, and claims to cure all his patients chiefly by regulating the bowel movements.

Of the many internal medicaments which have been recommended as helpful in acne, I will mention a few only. For many years it has been my practice to give my patients a tablet containing iron, ergot, and cascara, which are indicated in almost every case, for most of our patients are anemic and need some form of iron, almost all of them are habitually constipated and need a gentle, reliable cathartic, and the ergot not only exercises a stimulating effect upon the involuntary muscles of the uterus, but

also upon the involuntary muscles which control sebaceous activity. Based upon the idea of the disturbance of hormone secretions, a so-called dyshormony underlying this disease, various ductless gland extracts have been recommended. The extract of the corpus luteum seems to deserve a special place in many instances. Thyroid extract unquestionably has often a beneficial effect.

The general hygiene of the patient is of the utmost importance. It is a matter of daily observation that young men leading a strenuous physical life, who indulge in the rougher athletic sports, are free from acne. Tennis, basket ball, cold plunges, and swimming and rowing often help a great deal more than all kinds of medicines and vaccines.

Local Treatment.—This method is indispensable in almost all cases. Dr. George Henry Fox has for years preached and practised the use of the dermal curette. Properly employed, it removes with one sweep a great many of the comedones, tears open the superficial abscesses, and acts as an ideal surgical massage. This leads me to an important remark concerning the so-called facial massage as practised in many "beauty parlors." To a healthy skin, and used in a strictly sterile manner, it may not only do no harm, but may be of distinct benefit to the tone of the skin, but so frequently have I seen pronounced papulopustular eruptions following its use that I question its wisdom as a general routine.

The removal of the comedones is an essential part of the treatment. It is best accomplished by one of the various comedone extractors, all of which are based upon the same principle. My preference is for a small glass tube with a round, smooth, narrow end, built much like the former watch-key instrument, because it is so easily sterilized and permits, through ocular inspection, the observation of the actual work accomplished.

For the opening of pustules and deep-seated nodules I employ a fine, sharp-pointed, double-edged, special acne knife. The curette is my constant companion in treating these cases. In patients who are much averse to these surgical measures, much can be accomplished by touching the pustular and nodular lesions

with a mixture of phenol, iodin, and chloral, equal parts. This helps to destroy the surface lesions. The ordinary remedies which are useful in acne for their stimulating, antiseptic, and keratolytic effects are sulphur and resorcin, which can be used in 5 to 10 per cent. strength in a paste, salve, or lotion to suit the individual case. Much can also be achieved by the employment of so-called peeling or shelling pastes. In fact, many patients who for various reasons cannot submit to regular office visits, derive wonderful results from this plan. It consists in the application of strongly keratolytic agents, best in the form of a paste containing benzoinated lard, 30 grams; green soap, 20 grams; sulphur flor., 10 grams; resorcin, 6 grams; and betanaphthol, 2 grams. This is applied vigorously every night until there follows a marked irritation, when the treatment is temporarily supplanted by a soothing lotion or a mild cream, to be resumed again when the reaction has subsided. In this manner even a very severe case of acne can be cleared up, often within a few weeks.

Washing the face with hot water and a proper soap mornings and nights for a few minutes, using vigorous friction, followed by cold water, and finally firmly rubbing the face dry, is always useful.

Radiotherapy deserves special mention in this connection. On the wave of enthusiasm which followed the introduction of the *x*-rays in the treatment of skin diseases the profession was carried away beyond a point of safety. The beneficial effect of the *x*-ray in the treatment of acne is a matter of record, but much harm was done involuntarily at first. Many acne victims go about with the indelible destructive effects of overtreatment, such as atrophy of the skin with disfiguring telangiectases.

I have not abandoned the use of the Röntgen rays in treating acne; in fact, it constitutes one of my daily measures, but I try to use them wisely by employing weak doses carefully administered without producing a reaction. Used in such a way, and in connection with the other measures mentioned, they bring about rapid and perfectly satisfactory results.

One word as regards the use of face powders, as this is a regular question put to us by our lady patients. A simple dusting-pow-

der, free from poisonous substances, consisting best of pure starch, as, for instance, finely powdered rice with the addition of talcum, is perfectly innocuous, and on account of the hygroscopic action of the rice is, indeed, beneficial.

As acne constitutes almost 10 per cent. of the number of dermatologic cases in private practice, you will readily understand the enormous importance of properly and successfully managing these cases.

CLINIC OF DR. SOLOMON STROUSE

MICHAEL REESE HOSPITAL

DIABETES IN THE YOUNG

Successful Employment of Allen's Starvation Treatment in Children. Necessity of Careful Supervision of the Diet After the Patient Leaves the Hospital. Results of Modern Methods Compared with Older Methods. Prognosis More Hopeful at the Present Time. Significance of Renal Glycosuria in Children.

THE first patient I wish to show you today is this boy, ten years of age, who entered the Michael Reese Hospital on March 19, 1916, as a patient of Dr. Isaac A. Abt. He complained of marked thirst, increased appetite, increased urination, and loss of weight, with a duration of approximately three months. The family history is completely negative. Past history is also negative except for several attacks of tonsillitis.

As you can see, he is a large pale boy with considerable fat all over the body. Examination of the heart, lungs, and abdomen is negative; the reflexes are normal. In fact, the only abnormal finding in the physical examination is in the tonsils, which are extremely large, cryptic, and apparently filled with pus. He weighed on admission 80 pounds and 12 ounces.

The *urine*, on admission to the hospital, showed a large amount of sugar (5 per cent.) with intense reaction for both acetone and diacetic acid.

When he entered the hospital he was at first given a full diet and his urine showed the following characteristics: Amount in twenty-four hours 1650 c.c. (55 ounces); specific gravity, 1034; sugar (5 per cent.), $2\frac{2}{3}$ ounces; no albumin; acetone a large amount; diacetic acid reaction intense; ammonia, 1.78 gm.; microscopic examination negative.

On March 24th, the fifth day in the hospital, he was given 2 eggs, 300 grams (10 ounces) of 5 per cent. vegetables, 25 grams lean meat, and 25 grams wheat bread. The next day a slight but appreciable diminution in the excretion of sugar, acetone, and diacetic acid was noticed, and he was immediately placed on the "starvation" treatment for two days. On each day he received as much water as he wanted, 6 ounces of tea or coffee without sugar or cream every four hours, 2 drams of brandy every three hours, and 10 ounces of clear meat broth divided as he wished. The urine immediately cleared up remarkably, and at the end of the second day sugar and diacetic acid had disappeared and only a faint trace of acetone remained.

The diet was then increased gradually by the addition of eggs and vegetables, finally meat, fats, and other kinds of carbohydrates, until his discharge on April 21st. On discharge from the hospital his diet was as follows:

Breakfast.—One-half grape-fruit, 2 eggs, 25 grams ham, 5 c.c. cream, 5 grams butter, tea.

Dinner.—Stock soup, 100 c.c.; ripe olives, 2; lamb, 30 grams; lima beans, 50 grams; cabbage, 100 grams; sliced tomato, 50 grams; special ice-cream, 50 grams; tea with 10 c.c. cream; 1 almond muffin; butter, 5 grams; filberts, 10 grams.

Supper.—One egg; 1 almond muffin; tea; cream, 10 c.cm.; butter, 15 grams; carrots, 50 grams; cottage cheese, 50 grams.

During the day he also received 150 c.c. milk.

This diet contains approximately 60 grams protein, 115 grams fat, and 40 grams carbohydrate, with a total caloric value of 1435.

The urinary findings on discharge were as follows:

Amount in twenty-four hours, 900 c.c. (30 ounces), specific gravity, 1020; no albumin; no sugar; and a very faint trace of acetone. Ammonia was 0.44 gm.

On April 17th, when the urine had been sugar free many days, his blood sugar was 0.10 per cent., a normal value.

During the course of the treatment one interesting point developed which is worth emphasizing. The patient, being a spoiled boy, objected at first rather strenuously to the diet given, and as a result he surreptitiously ate only what pleased him.

At one time, about five days after sugar had disappeared, there was a reappearance of the sugar in the urine. This was undoubtedly due to the fact that on the day before the patient had suddenly decided to eat everything that was given him, and the change in the urine represented a sudden increase in carbohydrates rather than the gradual increase which had been planned and which we thought he was getting. This cleared up immediately when the cause was discovered and rectified.

The general physical condition of the patient remained excellent and was much improved when he left the hospital on April 21st. His craving for sweets had disappeared, he was perfectly happy with what he got, and had a sense of well-being that had not been present for months. His weight had increased 2 pounds.

The patient lives on the west side of the city, and the problem of after-treatment, of course, was the serious obstacle to a continuation of his good condition. Fortunately, his aunt, who has brought the patient to us today, had been carefully following the diet while the boy was in the hospital and volunteered to continue supervision. She had already been taught the meaning of the various terms used in the diet, and had been instructed in the use of food tables in the construction of menus. A few minutes only were necessary to demonstrate Haines' sugar test. She was then told to continue the diet the boy was having when he left the hospital, and to keep a book in which everything he ate, drank, and did was put down daily, and was instructed to bring the patient to the office for weekly observation. You will see by her note-book, which I shall pass around, how well she has performed her work.

As you can see from the condition of the patient today, the result of this coöperation is eminently satisfactory. We have not only been able to maintain the state of well-being, but we have been able to produce a gain in weight and an increased carbohydrate tolerance. The patient yesterday ate just what you can see in the note-book.

Breakfast: Two strips of bacon, 2 eggs, 1 bran muffin, one-half grape-fruit, and coffee with three teaspoonsful of cream.

At 10 A. M., one peach.

Dinner: Chicken broth (100 c.c.), steak (100 grams), one slice of bread (20 grams), baked potato (20 grams), rhubarb (90 grams) 1 bran muffin, one-half orange, and a cup of tea.

At 4 P. M., one apple.

Supper: One egg, 1 piece of French toast (equivalent to bread 20 grams and 1 egg), 1 radish, rhubarb 90 grams, cottage cheese 30 grams, 3 salted almonds, 10 strawberries, and tea with 5 teaspoonsful of cream.

This diet contains about 65 grams of carbohydrate. The boy now weighs $87\frac{1}{2}$ pounds, a gain of almost 7 pounds since treatment was started in March. The urine today contains no sugar, no acetone, and no diacetic acid.

To sum up this case, then, you see a healthy looking boy, aged ten years, who has no complaints about his health, who plays like other boys, who shows a completely negative physical examination, and whose urine would be accepted as normal by the most stringent life insurance examiners. In fact, the only difference between this patient and any other healthy boy lies in his food supply. He is abstaining from the sweets which boys and girls of his age are so apt to demand. Otherwise he is getting an ordinary fairly well-balanced ration. Contrast his present condition with the condition eight months ago, and you might well begin to wonder whether all cases of diabetes in children are rapidly progressive. Eight months ago he had an inordinate thirst and appetite, was passing large quantities of urine, and was restless and losing weight. His urine then contained much sugar, acetone, and diacetic acid.

What, then, are the lessons to be learned from this patient? In the first place, he came for treatment early in the disease at a stage when theoretically at least a minimum of damage had been done to his system. We know from our experience with diabetes in older persons that considerable prognostic importance must be attached to the stage at which treatment is begun, and there is every reason for believing that this should likewise hold true with children. It is generally accepted as true that the younger the patient is, the more likely is the diabetes to be severe, and we know that in a severe case of diabetes treatment begun early offers a

better prognosis than later treatment. Therefore in this patient our ability to begin treatment early was of material benefit to him.

Then you will notice that after treatment was actually started it required only three days to make the patient aglycosuric, and it is an axiom that the quicker we free the urine from sugar the easier will it be to continue successful treatment. In this patient, as in others which I shall discuss later, Allen's starvation plan has worked very well, just as has been reported by other men treating diabetes in children. The difficulties of freeing the urine of sugar are not always so easy to overcome, yet success in this effort is necessary as the first step in treatment. This boy did not seriously object to the starvation days, especially as we took pains to put something into his stomach at frequent intervals; the broth, coffee, wine, and water at least made him feel as if he were being fed. The second stage of treatment, the stage of testing tolerance, was not so easily passed because of the patient's dislike for certain of the foods offered him and his silent refusal to accept them. But when this was discovered, a little diplomatic manipulation of promises for the morrow made our patient amenable to reason, and he then very willingly ate the disliked vegetables as a bond for his special ice-cream the next day.

At this point I think it well worth while to emphasize the necessity of going slow when testing out tolerance. You all know the details of the Allen method so well that I would waste your time going over them, but I do not think too much emphasis can be laid on the advantages of feeling one's way slowly. Even if a few days are added to the patient's period of observation, time is saved in the long run, because gradual additions to the diet will often prevent the return of glycosuria, and the appearance of glycosuria always spells delay.

But perhaps the most important lesson this youngster teaches is learned after he left our direct supervision in the hospital. Where we formerly made no very deliberate attempt to instruct the patient as to how to care for himself, we now devote a considerable part of his hospital stay to such instruction. When a diabetic leaves our care in a hospital today he usually knows about as much concerning nutrients and caloric values, the appearance

of sugar and its significance, as does the doctor. He also knows the significance of each article of diet and what to do in case sugar appears in his urine. He has become interested in the game of getting well, and takes care of himself in a way that surprises the physician. This is quite in contrast to what he did formerly.

It would seem almost hopeless to instruct children in after-care, but it seems to me that undoubtedly at least part of the bad results in children may be attributed not so much to the inherent severity of the disease as to the difficulty of making a child and his family obey orders. If present methods are to be any more successful in raising hope for the diabetic child than were former methods, certainly the most important factor will be the instruction of the responsible party in the care of the child.

With wealthy people who can afford constantly a trained nurse or trained maid this care can easily be obtained, but with the less fortunate patients—where often even the mother is working—it is an extremely difficult problem to be able to carry out any successful line of treatment. Yet I am sure that this will be absolutely necessary. As successful as the Allen starvation method has been with this boy and in other cases reported in the literature, it by itself cannot hope to improve the prognosis in children unless we can control the post-hospital treatment as efficiently as we can that of the adult. If we can do this and prevent the child from taking liberties with his diet, I see no reason why children should be as uniformly subject to diabetic coma as they seem to be. In adults the newer methods have made diabetic coma a rarity. It is not necessary to assume that the disease in children is inherently different from that in adults. It is, of course, probably true that the problem of growth and development complicates the situation, but it is also apparent that the difficulty in continuing treatment outside an institution is an important factor.

To strengthen these points allow me briefly to refer to another lad from out of town, whom I also saw through the courtesy of Dr. Abt. He was thirteen years of age when he entered the hospital on October 19, 1915, remaining until the 29th of November. He had the usual symptoms of diabetes of two months'

duration and his physical examination was completely negative. On admission he was passing on a carbohydrate-free diet 1 ounce of sugar and a trace of acetone, but he was easily made sugar free after three days of starvation. For thirty-eight days following this the patient remained sugar and acetone free except for four test days, when extra carbohydrate was added to the diet. On discharge he was getting about 60 grams of protein, 115 grams of fat, and 70 grams of carbohydrate, with a total caloric value of 1555.

Reports received from this patient since leaving the hospital show a continuance of the good condition. He is free from sugar and acetone and is gaining weight. The only difference between this boy and the one just shown is to be found in the greater difficulty experienced in teaching his mother the fundamentals for carrying out the diet and the plan of life outlined. At first when he went home he did not get along as well as he did while under our direct care, which was due almost entirely to the fact that I had not given specific enough instructions to the boy's mother. In practically every other detail the cases are identical, yet this boy threatened to turn out in quite a different way until a second personal interview with the mother cleared up the obscurities of my previous instructions. This certainly emphasizes the point already made of the extreme necessity of full co-operation between physician and some responsible party if good results are to be obtained in treating diabetes in children.

Both these patients may be considered as mild cases, so I shall now refer to a third patient with a more severe type of the disease.

A girl aged eleven years, from out of town, referred to me through the courtesy of Dr. Abt, entered Michael Reese Hospital on September 1, 1915, complaining primarily of marked loss of weight and secondarily of the usual symptoms of diabetes. In January, 1915, the symptoms had started with a craving for sweets and an increased appetite. Two factors, perhaps of importance, should be mentioned as preceding these symptoms: First, the Christmas holidays with the usual abundance of sweet foods and candy, and, second, a very severe attack of tonsillitis just preceded the symptoms.

All through the winter of 1915 the patient progressively lost weight, but a diagnosis was not made until August. In August, 1915, the diagnosis of diabetes having been established, the patient was placed by her physician on a diet containing a minimum of carbohydrate and a maximum of protein. This diet had no noticeable effect on either the symptoms or the urinary findings.

When the patient was first seen by Dr. Abt the urine contained about 5 per cent. sugar in the afternoon specimen, with both acetone and diacetic acid present. The physical examination was negative except for the loss of weight and the flushing of the cheeks. Both family history and past history were unimportant.

It happened that on the day the little girl came to Chicago she became nauseated and ate nothing for twenty-four hours. She entered the hospital the next day, and the urinalysis after the self-imposed starvation surprised every one, as for the first time since the diagnosis was made no sugar was present. Therefore it was quite natural to continue treatment along the same lines as have already been outlined in the discussion of our first patient. Unlike the boy, however, it was found that this child had a very low tolerance not only for carbohydrates, but for proteins as well. As long as the diet consisted of nothing but eggs and vegetables she remained sugar free with only a trace of acetone. But the addition of even the slightest amount of starchy foods in any form produced glycosuria. Likewise we found that even as small an amount of animal protein as 10 grams of meat resulted in glycosuria. This, of course, made the problem of the diet extremely difficult, since the protein intake had to be limited as well as the carbohydrate. Buttermilk was fairly well tolerated, and a diet was finally constructed consisting of the following:

Breakfast: One-half grape-fruit; 1 egg; 2 strips bacon; 1 almond muffin; tea.

10 A. M.: Celery, 40 grams.

Dinner: One egg; 2 strips of bacon; egg plant, 50 grams; sauer kraut, 50 grams; celery and nut salad, 50 grams; 1 almond muffin; tea.

3 P. M.: Nuts and celery.

Supper: One egg; cream of celery soup, 100 c.c.; caviar and

cheese (small amount of each); asparagus, 100 grams; 1 almond muffin; bread, 10 grams; tea.

8 P. M.: One almond muffin; buttermilk, 180 c.c.

On this diet the urine showed these characteristics: Amount in twenty-four hours 1400 c.c. (46 ounces), specific gravity 1015, no sugar, no acetone, and no diacetic acid. Any increase in diet produced glycosuria and the appearance of acetone. Starvation days were used once a week. She gained about 5 pounds under treatment, weighing 64 pounds on admission and 69 on discharge.

She left the hospital on October 5th, but remained in Chicago under observation until early in November. During this time the basal diet just outlined was continued and frequent attempts were made to test tolerance, but by the end of a month there was no evidence of increased tolerance for either proteins or carbohydrates, and by this time a very marked tendency to acidosis occasionally manifested itself.

The patient had a nurse who was co-operating with us, and it was decided around the first of November to take her home, where during the next few months the principles just outlined were continued. By this time a slight improvement was noted and the patient's parents took her to another hospital, where tests for tolerance showed a slight definite increase over what had been present when she was here. The patient's diet on returning from the hospital contained 80 grams of protein, 130 grams of fat, and 35 grams of carbohydrates, making a total of 1634 calories. She weighed 65¼ pounds, and the urine was free from sugar and acetone. She was exercising freely and, except for the lack of gain in weight, she seemed a normal child, although glycosuria appeared as soon as the limits of diet were transgressed.

From that time until today there has been a slow but steady improvement in the patient's condition, which has been manifested not only by an ability to handle more food, but by an improved condition in the urine, and recently a slight gain in weight.

Although the story of this little girl does not sound so different from the story of the two boys, the actual management of the case was quite different. With the boys the usual treatment for mild diabetes brought excellent results; with the girl an extremely

low tolerance for both protein and carbohydrate and an ever-threatening acidosis kept us continually on the alert. In studying the whole history of the case I cannot help feeling that certain very definite factors played an important rôle in creating or at least intensifying the difficulties. In the first place, you will remember that the girl had diabetes seven or eight months before a diagnosis was made, and that by the time treatment was instituted she was already severely ill. During all these months there was no restriction of either carbohydrate or protein, which by itself would certainly tend to make any case of diabetes in a child severe. The point has already been made in the discussion of the other cases that early diagnosis makes for a better prognosis, and the history of this patient surely emphasizes this.

But by far the most important and most valuable lesson of this case lies in the final improvement. After almost a year of the most painstaking care by the family the little girl is in better condition than she was when I first saw her last September. Without this constant supervision the disease must certainly have progressed to a fatal end, and although an ultimately favorable prognosis cannot be given, it is a long step in advance to be able to promise the improvement this patient has shown.

Before going over the next patient I should like to try to answer two questions which probably have arisen: Have these results been due to modern treatment? What is the final prognosis? To answer these I should like to refer to some previous experiences with similar cases before we were using exactly present-day methods of treatment. I recall a boy thirteen years of age who entered the hospital on February 20, 1913, with a history of the usual symptoms of diabetes of two months' duration, with especially marked loss of weight. The physical examination was negative, and there was nothing of importance in his family or past history.

On admission to the hospital the urine showed 5 per cent. sugar, a tremendously positive acetone reaction, and a positive diacetic reaction. He also showed some clinical manifestations of a beginning diabetic coma; that is, he was somewhat drowsy, complained of headache, and had a rapid pulse.

Using the principle of the gradual reduction of carbohydrate in combination with vegetable days and von Noorden oat gruel, in six days he became sugar and acetone free. He was treated until May, 1914, during which time there was a steady increase in tolerance and a steady gain in weight, so that during this period the patient's mother was able to take out some life insurance for him. The only times sugar appeared during this long observation were when the boy overstepped the bounds of his diet and stole sweets. Incidentally, every time he did this, not only did sugar appear in his urine, but a marked acetone reaction was present, and the difficulties of getting him sugar free were increased by each offense.

Finally, the boy went on a real "carbohydrate spree," immediately went into coma, and died on May 16, 1914.

Two other boys, aged eleven and thirteen, were treated in 1910, with almost identical results, complete clearing up of the urine and disappearance of all symptoms, but both died in diabetic coma which followed almost immediately excessive indulgence in stolen sweets.

These three earlier cases all showed as good an immediate result as the three later ones. You may recall how writers at the time were maintaining that the von Noorden oat gruel was especially successful in children, but they all must be classed as mild cases. It is, therefore, impossible on the basis of the material at our command to judge whether the newer methods will be any more successful than the older ones in children, especially in the milder cases, but by analogy with adult diabetes, and from a theoretic standpoint, it seems to me that the starvation treatment has the same indications with children as it has with adults.

As regards the ultimate **prognosis** we can only guess. Diabetic children usually die in coma following overeating, and diabetic coma is becoming less frequent as methods of treatment improve. The plan of testing tolerance for all components of the diet, and of having a more intelligent coöperation between a responsible person and the physician, would surely seem to offer more hope of averting coma; but whether a child can be kept in a state of undernutrition for a period long enough to improve the

diabetes without seriously impairing development is, of course, a question for the future to decide. I have seen no diabetes in infants, where the feeding problem is essentially different from adults, but I doubt very much if any method can offer improved prognosis in such cases.

But in older children we can well consider the possibility that the disease is not inherently different from diabetes of older persons, and that the gloomy prognosis is caused at least in great part by no insurmountable difficulties in the practical handling of the case.

It is true, as Joslin says, that practically the only cases of diabetes in children which have survived have been those in which there is a familial tendency to the disease, and, of course, with the basis of years of experience against one it is hazardous to suggest any other outcome. With modern experience as limited as it is, it would be the height of folly to say that diabetes in children need not necessarily be fatal, but the experiences nevertheless point to a decidedly more hopeful prognosis than heretofore, provided there is the opportunity for early treatment and for continued treatment. The little girl whose history I abstracted had a severe diabetes at the outset, but she is now certainly not a rapidly fatal case, and this improvement is just as certainly due to the care which she has had. Our other cases are doing remarkably well, are all showing an increased tolerance, an increase in weight, and are apparently growing in the normal healthy way.

Notes on Subsequent Histories

Late reports on these patients confirm in detail the conclusions expressed. Our first patient continues on the highway to health. The second, the boy from out of town, has suffered continued reverses, all of which may be traced to indiscretion and indifference on the part of his mother. Instead of following the advice given her, not only by us but by other physicians, and instead of paying attention to the details outlined, the mother has been careless. As reported to us the patient is now having a hard time. On the other hand, I saw last week the little girl, and was surprised to find her looking extremely well, although thin. Her urine was free from all pathologic constituents, and she was really "enjoying life."

A CASE OF RENAL GLYCOSURIA

Now let me show you an example of a rare anomaly characterized by glycosuria. This healthy looking boy is thirteen years old; he was referred to me by Dr. Heliodor Schiller. He gives the following history: About three weeks ago he was in Michael Reese Hospital in order to have a tonsillectomy performed. He had had several attacks of tonsillitis in succession, and in several of these attacks his urine had been examined by Dr. Schiller and nothing abnormal found. On the day of operation the routine urine analysis showed sugar, and operation, therefore, was deferred. Dr. Schiller put the boy on a reduced diet, but the trace of sugar remained, and rather quickly acetone appeared.

I first saw him on May 9, 1916. He gives none of the characteristic symptoms of diabetes. He feels perfectly well and his only complaint is the frequent attacks of tonsillitis. As you can see, the boy is a very well-developed lad for his age and shows a rather definite increase in fat. The tonsils are enlarged and scarred. There is no pubic or axillary hair, and in some respects he has the appearance of hypophyseal disturbance. His intelligence is perfectly normal and physically he is an active athlete.

On May 9th, after three weeks of carbohydrate-free diet, his urine showed the following: Specific gravity 1023; reaction acid, trace of sugar, no acetone, no albumin, and negative microscopic findings. The amount of sugar present was too slight to be determined by ordinary clinical procedures. The urine was fermented by yeast and turned the plane of polarized light to the right, the reducing substance evidently being dextrose. The blood-sugar determination, made one hour after a full meal rich in carbohydrates, showed .04 per cent.

From that time until now the patient has continued to eat everything he cared for except sugar, and at no time have any symptoms of diabetes manifested themselves. Despite the pro-

longed ingestion of carbohydrates the urine today shows the same trace of sugar, apparently no more and no less than was present when the patient was on a carbohydrate-free diet.

This is apparently a case of so-called renal glycosuria, the diagnosis of which is established first by the absence of clinical manifestations of diabetes; second, the constant excretion of a small amount of sugar practically independent of carbohydrate intake; and, third, the low blood-sugar value.

A few years ago Salomon described, under the name of "Diabetes Innocens of the Young," a group of cases in which the usual severe picture of diabetes was not seen. Some of his cases, however, were not in young folks and were apparently merely mild diabetics. Others belonged to the group known as "renal diabetes," to which this patient belongs. The recent interest in renal glycosuria, as it should be more properly called, has demonstrated that there are cases of glycosuria in the young of an innocent nature. These are characterized by the appearance of sugar without relation to intake of carbohydrate, by a low blood-sugar content, and by a history which shows no tendency to manifest the true symptoms of diabetes. Such cases, when discovered, need not be treated as diabetes, and, as a matter of fact, stringent dietetic regulations are decidedly out of place, as this is not a true metabolic disorder.

I have had one such patient under observation now for a number of years, a young man who at the time of the initial observation was twenty-one years old. He is now married and has a child. He has gained tremendously in weight, enjoys perfect health, but constantly passes a trace of sugar no matter what he eats or does.

Another group of cases in which sugar may appear in the urine is the group of alimentary glycosurias. In these, sugar appears as the result of an excess of sugar or starch in the diet, and disappears upon the removal of this cause. Such cases represent merely a tendency toward a low sugar tolerance, and while it is true that very early cases of diabetes may show nothing but alimentary glycosuria, it is likewise true that most cases of alimentary glycosuria, when kept under observation, do not develop diabetes.

It sounds like a platitude to say that before treating diabetes the diagnosis must be absolutely established. The mere presence of a reducing substance in the urine is never a sufficient basis for diagnosing diabetes. This reducing substance must, first of all, be identified as dextrose by the usual chemical means at the disposal of any clinical laboratory, and even then further steps should be taken to clinch the diagnosis. The determination of blood-sugar can easily be done today and should be performed in every case of glycosuria. Furthermore, the clinical history, development of the symptoms—thirst, increased appetite, increased urination, the relation between intake and excretion of sugar—and the course of the disease must all be carefully observed before labeling a glycosuria as diabetes. And until we use every possible means of making a diagnosis, and are thereby sure that the reducing body means diabetes, we must be cautious in discussing prognosis and treatment. Although glycosuria is presumptive evidence that the case is diabetes, it is not any more positive proof than a continued fever is positive proof of a typhoid infection. Treatment of a case of renal glycosuria as diabetes would be bound with unnecessary difficulties for the physician and unnecessary hardships for the patient, and an unwarranted gloomy prognosis would have to be given. I think we are fortunate today in having this boy with us to bring home this warning.

CLINIC OF DR. JOSEPH C. FRIEDMAN

MICHAEL REESE HOSPITAL

CHRONIC DIARRHEAS

Three Cases Illustrating the Common Types of Diarrhea Seen in Temperate Climates: (1) Chronic Severe Colitis, (2) Mucous Colitis, and (3) Achylia Gastrica. Technic and Interpretation of Stool Examinations. Principles of Treatment: (1) Removal of All Irritation from the Intestine, (2) Combating the Inflammatory Process. Careful Dietetic Management Necessary in All Cases.

THIS young man is twenty-eight years of age, married, a salesman by occupation. His trouble began about three years ago, when he noticed long strings of mucus adhering to the outer part of the stool, and about six months later the present diarrhea set in with stools varying from six to fifteen daily. Stools are very small in amount, sometimes containing fecal matter with pus and blood, and sometimes the latter alone. The first stool in the morning is more solid than the succeeding ones. The second, perhaps fifteen minutes later, contains much mucus. No particular relation to meals is noticed, and no pain of any sort before a bowel movement, the only discomfort being at the anal ring. His appetite is good, but he tries to be careful about his diet. He has not lost in weight.

He has never been sick before, with the exception of an attack of gonorrhea some years ago. Family history is negative. His habits are good. He has always lived in Chicago.

Physical examination shows a well-nourished, muscular young man. The thyroid is not enlarged. The chest is normal. Abdominal examination reveals no abnormal peristalsis. The

spleen is just palpable at the costal arch. Its edge is sharp and hard. There is some tenderness on deep pressure along the course of the descending colon. No tumor is palpable. A right-sided inguinal hernia, easily reducible, is present. Reflexes are normal, pulse 70, and temperature is normal, and has been so during his stay in the hospital. Blood examination shows a hemoglobin of 90; red blood-cells, 4,480,000; whites, 6400; differential, 62 per cent. polynuclears, 38 per cent. mononuclears and transitionals; no eosinophils seen. The Wassermann is negative. The urine is normal. To this point, then, the findings are quite negative, except for a chronic splenitis and the colonic tenderness, which latter, of course, is common enough in all types of diarrhea.

Proctoscopic examination showed a hyperemic, thickened, granular, easily lacerated mucosa, streaked with masses of pus and mucus. A number of narrow, rather deep ulcers, with irregular, not undermined, edges were seen in the ampulla. *x*-Ray examination with bismuth by mouth and per rectum showed nothing abnormal except an apparently local spasm just above the rectal pouch.

Stomach contents show normal acidity (39 free and 55 total), normal motility, and no increased mucus. I have here a specimen of stool. It is small in amount, green in color. Its reaction to litmus is alkaline; as it is already watery, it is unnecessary to grind it up in a mortar for further examination. We simply pour some in a Petri dish, cover it, and hold it toward the light to disclose the large masses of translucent yellowish material which in a stool mean invariably either cellulose or mucus. If the latter, they are stringy and adhere to the dish when pulled with a forceps. If the former, they are much more firm. Here there is no doubt about their being mucus, but we nevertheless place a piece under the microscope and stain with a dilute iodin solution, such as Lugol's. Mucus, as is the case here, shows innumerable finely granular parallel striæ, while cellulose is shown to consist of the individual vegetable cells with yellow stained cell membranes. Microscopically, we see also iodin-stained epithelial cells, pus corpuscles, and numerous red blood-cells.

No ova or parasites are seen. We have repeatedly examined fresh stools, kept warm, for amebæ, and many others for tubercle bacilli, without success. The interpretation of this stool examination is simple. A small alkaline stool, with large masses of mucus, not intimately mixed with fecal matter, invariably points to an inflammatory process of the large bowel, and the smaller and more frequent the stool, the lower down the process. The presence of pus and blood points to a process involving the deeper layers, so that the diagnosis in this case from the stool examination is a rather severe colitis, but nothing is revealed as to its etiology, and clinically it is, of course, extremely chronic.

By making sure that the process is taking place in the large intestine and is markedly inflammatory in type, we can immediately rule out a number of the causes of primary chronic diarrhea, including the gastrogenic group, *i. e.*, achylia gastrica, the ductless gland group, including the pancreas, thyroid, and adrenals, insufficiency of which can produce diarrhea, which, however, practically never involves the large intestine alone, and simple nervous diarrhea. We have left, then, as possible causes the secondary diarrhea due to cardiac and renal conditions, which are absent here; the chronic dysenteries, amebic or bacillary; carcinoma of the large intestine; tuberculosis or syphilis of the colon, diverticulitis, and the severe types of chronic colitis of unknown etiology. The methods of deciding between these are those already used. Examining the warmed stool for amebæ is always important, for sporadic cases of amebic dysentery may occur anywhere, and should be considered, no matter how atypical the history or how apparently mild the colitis, for a chronic amebic dysentery occasionally shows no pus or blood, simply mucus. Here amebæ are certainly absent. Tuberculosis of the gastrointestinal tract can, of course, be demonstrated only by finding tubercle bacilli in the stool. It is not nearly so frequent as assumed. Cabot has shown from the Massachusetts General Hospital autopsy records that even when patients with advanced pulmonary tuberculosis get a diarrhea it need not be tuberculous, *i. e.*, it may be a simple gastro-enteritis; and second, when there is a demonstrable tuberculosis of the colon, in only 1 case out of 3

is there a diarrhea. Examination of the stools here by concentration methods were repeatedly negative. Carcinoma of the large intestine, though unlikely at this age, is, of course, not impossible, it being a well-known fact that carcinoma of the intestinal tract occurs relatively frequently in the young. Against this assumption is the history, which is not that of a chronic obstruction, the latter being an increasing constipation, alternating with diarrheal attacks following the use of cathartics. No carcinoma was found with the proctoscope or the *x*-ray. Mucous colitis is also easily ruled out. It is a superficial process involving only the epithelial layer. It occurs in nervous, constipated individuals—*i. e.*, is partly nervous and partly inflammatory, but never involves the deeper layers to the extent of having large amounts of pus and blood in the stool, as in the present case. Syphilis of the intestinal tract is very rare, but must be thought of in cases of chronic diarrheas where no other etiology can be found. It is certainly absent here. Diverticulitis should be considered, as it accompanies colitis occasionally, and, of course, can be demonstrated only by the *x*-ray or laparotomy.

After ruling out the above, we have left only the group under chronic colitis of unknown and probably varying origin. Some cases, perhaps more frequently in old people, follow a gastroenteritis, some following repeated exposure to sudden changes in temperature, as in men who work in the ice-houses of packing houses and pass from warm to cold frequently, but the majority give no clue to the etiology. They have a diarrhea, with frequent small stools, containing first mucus, then pus and blood, and get better and worse, and so on.

Various theories have been proposed to explain these cases. The gas bacillus has been accused of being the only cause, as well as the streptococcus, from distant foci of infection. I see no reason for presupposing a single etiologic agent in all cases any more than we need do so in chronic gastritis. If we have dietetic errors, or chilling, or any acute infection causing acute colitis, then it is easy to understand why, with the myriads of bacteria and with the constant irritation of the fecal matter at hand, the infection is kept up and extended to the deeper layers through lymphatics

and gland ducts, until we have a condition like chronic gonorrhea in its persistence. The part played by the presence of fecal matter may be better understood when we remember that, although the small intestine is five to six times as long as the large, yet food passes through the former in three to six hours, taking at least twenty hours in its passage from cecum to anal ring. This perhaps partly explains why chronic and deep inflammatory processes are so much more frequently localized in the large intestine.

Pathologically, we have two varieties, distinguishable only at autopsy: the ordinary ulcerative colitis, a chronic process, involving part or all of the large intestine, and the non-ulcerative, or granular hypertrophic, type. As an example of the latter and rare form, I show you this specimen of colon. The patient was fifty-six years of age, a widow, had stomach trouble for eight years with nausea and vomiting (she was an alcoholic), and recently has had frequent small stools daily, with pus and blood. Proctoscopic examination showed the same condition as in the patient just shown you. She had an old perforation of the soft

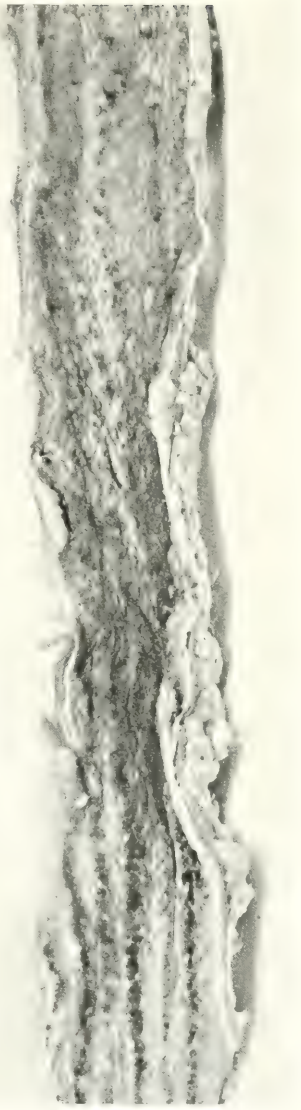

Fig. 53.—Granular hypertrophic colitis. Note the longitudinal striæ capped by the darker hemorrhagic areas.

palate. The stomach contents showed absence of free HCl, total 7, no lactic acid, much mucus, and good motility—evidently an atrophic gastritis. The Wassermann was negative. She was put on a diet with dilute HCl by mouth, but did not improve. Then mercury inunctions were begun in spite of the diarrhea. Improvement was rapid and progressive until she developed a facial erysipelas and died. As you see, the whole colon is involved, the process stopping quite abruptly at the ileocolic valve. The whole intestine is thickened, the mucosa hypertrophic, and the descending colon is marked by longitudinal ridges capped by hemorrhagic areas. There is not a single ulcer present, and yet pus and blood were constantly present, evidently simply from the unbroken mucosa. This is probably a simple chronic granular colitis in an individual whose resistance was lowered by alcohol and syphilis, and shows us that the presence of pus and blood in the stool, even in large quantities, does not justify us in diagnosing an ulcerative colitis.

The prognosis of these cases as to life is, on the whole, good. Few die from the immediate effects of the colitis, about 50 per cent. are cured ultimately, and the remainder have periods of improvement alternating with relapses for almost indefinite periods.

Of the treatment I shall speak later.

The second patient I wish to show you is this man, aged fifty-seven, a carpenter, married, who for the last ten months has had a diarrhea, with three to seven stools daily, beginning as soon as he awakes in the morning, with stools immediately following each meal, and sometimes between meals. Stools are large, soft, and do not, to his knowledge, contain mucus or blood. He has no pain preceding or with stool, but he has at times distress in the epigastrium. His appetite is good and there has been only a slight loss in weight. He does not complain of cough or night-sweats and has always been healthy, without intestinal disturbance of any sort, before the present attack.

Examination shows a fairly well-preserved man, with normal lungs, normal heart outlines, and a slight systolic murmur at the apex following the first sound (sclerotic valve?).

There is no abdominal tenderness anywhere, no tumor, or

abnormal peristalsis. Rectal examination is negative. The reflexes are normal. Urine, blood, and blood-pressure are normal.

We have here a specimen of stool. It is in marked contrast to the other in size, being very large, light yellow, and unformed, with numerous coarse particles in it. Grinding up a little in a mortar with some water we pour it in a Petri dish, and see a number of rather large, translucent masses which are quite firm when pinched with forceps, and some very small masses which resemble the mucus in the previous case. Placing specimens of both under the low power and staining with iodin, we see the cellular structure of the larger particle, showing it to be cellulose from vegetable or fruit, while the finer masses have the parallel striæ and finely granular appearance of mucus. Another drop of stool stained with iodin reveals some meat fibers with the transverse striæ still clearly visible, showing that they are not well digested, some blue-stained starch granules, and numerous small, pointed crystals which are fat crystals—*i. e.*, fat which has been broken up by pancreatic ferment. Another drop stained with Sudan III shows some increase in red-stained fat globules. No epithelial cells, pus-corpuscles, or ova are seen. As we see no red blood-corpuscles, it is necessary here to make a chemical test for blood. Taking about 6 c.c. of ground-up stool, we add one-third the volume of glacial acetic acid, shake well to form acid hematin, add an equal volume of ether, in which the hematin is soluble, and pour rather carefully a number of times from one tube to another, in order to extract all the hematin and yet *not* take up too much pigment. Allow it to settle, and then pour off about 5 c.c. of the ether extract. To this is added about 15 drops of a freshly made saturated solution of tincture of guaiac and 2 c.c. of hydrogen peroxid. In the presence of hematin the guaiac is oxidized to a blue pigment. If much bile pigment has been extracted instead of the blue, we are apt to get a purple or red color, making the reaction very doubtful. As a control we may use the benzidin test, done exactly the same way, only using tincture of benzidin instead of guaiac, and getting a green color instead of blue. It is very much more sensitive than the former, revealing blood in a dilution of 1 : 80,000 instead of 1 : 10,000.

It is so delicate, indeed, that many reject it as useless for clinical purposes, but under the above conditions—viz., when the guaiac is doubtful—a very strong benzidin is of considerable help.

A word here as to errors in chemical blood-tests. It is generally stated that bismuth and inorganic iron by mouth will give a positive blood-test in the stool. This, I think, is wholly fallacious, as the inorganic salts of these metals are not soluble in ether; second, the danger of positive tests when the patient has meat in his diet is greatly exaggerated. Unless the patient has a diarrhea or has taken considerable quantities of underdone meat, it is rare that removal of meat from the diet will change a positive guaiac test into a negative, though it may occasionally do so to the benzidin test. This source of error must always be thought of, however, though it is not a frequent one. The blood-test in the present instance is clearly negative, in spite of the presence of some undigested meat-fibers.

The interpretation of the stool examination, then, is as follows: The large size points to a process in the small intestine, as do the fine particles of intimately mixed mucus. The undigested cellulose, starch, and meat fibers may mean either that the food was hurried so rapidly through the intestines that there was not sufficient time for digestion (a condition found in the lienteric stool of acute gastro-enteritis), or it may mean a pancreatic insufficiency. Against this assumption the small amount of unchanged fat globules speaks, the numerous fat crystals representing fat which has already been broken up by the pancreatic juice. The absence of pus and blood and the presence of a slight increase in mucus point to a slight superficial inflammation.

We have, then, a process in the small intestine, accompanied by increased peristalsis and a very slight superficial inflammation.

The stomach contents in this case are interesting. The tube was introduced forty-five minutes after a test-breakfast and nothing obtained. It was introduced thirty-five minutes after a second test-breakfast, and 60 c.c. of a thick, poorly digested mass was withdrawn, which contained no increase in mucus, no free HCl, a total acidity of 10, no lactic acid, and no blood;

in other words, a typical achylia gastrica, or absence of hydrochloric acid secretion.

The *x*-ray examination verified the clinical findings, showing an orthotonic stomach which emptied itself unusually rapidly, the same rapid advance being in evidence along the rest of the intestinal tract.

The final diagnosis of this case is clear from the following consideration: We may at once rule out the inflammatory conditions of the large bowel from the stool examinations. The chronic dysenteries, mucous colitis, granular and ulcerative colitis, the severe inflammatory conditions of the small bowel, such as carcinoma and tuberculosis, are also disposed of by the absence of pus and blood and large amounts of mucus in the stool—*i. e.*, the absence of signs of severe inflammatory conditions. Parasites are absent in the stool. Syphilis is improbable because of the absence of any indication in the history and a negative Wassermann. The diarrheas more particularly affecting the small intestine are left. First the ductless gland group, the thyroid and suprarenal glands, are easily excluded. A pancreatic insufficiency must be seriously considered. It causes these large stools, but cannot be the cause here because of the very small number of fat globules in the stool. The fat present is practically all in the form of fat crystals, showing that the fat-splitting ferment of the pancreas must have been secreted to break up the neutral fats. Had there been any doubt on this score, we could have passed the Einhorn duodenal tube and aspirated the duodenal contents and so demonstrated trypsin and steapsin. We have left, then, a nervous diarrhea and the gastrogenic group. It is easy to decide between these, as the man is certainly not a neurotic, and, secondly, repeated examinations of the stomach contents showed invariably no free HCl and a total of not over 10. We shall not enter here into a discussion of achylia gastrica. Suffice it to say that it may be the expression of a carcinoma of the stomach or an end-result of an atrophic gastritis, neither of which is present here from the absence of mucus, blood, and lactic acid in the stomach contents. Achylia from pernicious anemia and other severe general conditions is, of course, ruled out by the physical findings. Lastly, it

may be a functional achylia, which is apparently the case here. We call these cases functional because many of them are surely simply cases of congenital weaknesses of the secretory apparatus of the stomach, and in some of these, after many years of achylia, free HCl has again been found in the stomach, while other cases have apparently an anatomic change in the gastric mucosa—*i. e.*, a granular gastritis as their basis, and are, of course, not strictly functional. However, they are benign, may remain latent for many years, and may then give rise to gastric symptoms, most frequently a feeling of fulness and belching immediately after meals, or intestinal symptoms, most frequently by far a diarrhea of the type our patient complains of, but occasionally an obstinate constipation. The patients not infrequently lose moderately in weight, practically never become cachectic, and the diarrhea has the characteristics, first, of beginning in the early morning; second, of occurring very soon after the ingestion of food; third, of consisting of very large stools, unless, as occasionally happens after the condition has lasted a long time, a secondary colitis is set up, when large bowel stools may result. The cause of these gastrogenic diarrheas is obvious. One of the functions of the stomach is by means of HCl to prepare the connective-tissue framework of meat, vegetables, etc., so that under the influence of the alkaline pancreatic juice it is rapidly dissolved, leaving the parenchyma in small masses, easily dissolved by the intestinal juices. When, however, the stomach function is in abeyance, large masses of food are passed through the small intestine and, of course, act as irritants, stimulating peristalsis, and, as stated above, at times giving rise to real inflammatory conditions with increased secretion of mucus, etc. The proof of this lies in the therapeutic test, to be mentioned later. The prognosis in these functional achylias is excellent. They are very amenable to treatment, almost equally as much as the functional hyperacidities.

The third patient I shall spend but a very short time on. His complaint is epigastric distress three to four hours after eating, with attacks of diarrhea of ten to fourteen days' duration, averaging three to four large liquid bowel movements

daily, containing large amounts of coarse mucus with no visible blood or pus. The bowel movements are not preceded or accompanied by pain. He is rather constipated between attacks, is very nervous, and was under a severe mental strain at the onset of this illness. He had always been healthy before.

Physical examination reveals nothing of importance—a normal chest, slight tenderness on deep pressure in right and left lower abdominal quadrants, no tumors or peristalsis, deep reflexes slightly exaggerated, and very marked vasomotor skin phenomena. Unfortunately, I cannot show you a specimen of the stool described by the patient, as he is about ready to go home, but it consisted during the height of the attack of large masses of grayish-white mucus, at times unmixed with feces. Microscopically, the mucus contained large numbers of epithelial cells and some pus corpuscles embedded in it, but no blood. The stool contained no undigested food particles. We can interpret the laboratory findings, then, as a superficial inflammatory process, involving probably a large part or all of the large intestine, the liquid stool testifying to the involvement of the ascending colon, while the small intestine is probably free, there being no undigested food particles, either macro- or microscopically. Proctoscopic examination revealed nothing abnormal. The *x*-ray was negative. Stomach contents showed no free HCl, and total of 22 to 30; no lactic acid, blood or mucus, and good motility.

To sum up, then, we have a markedly neurotic individual who, after a prolonged mental strain, develops a diarrhea with tremendous amounts of mucus occurring at intervals, the stools being relatively free from it between attacks. This is quite in agreement with the definition of mucous colitis, which I believe this case to be. The hypo-acidity has no etiologic relation to the diarrhea. It is not an achylia, and is, I believe, simply a result of his generally depressed functions.

These three cases are, I believe, the kinds one sees most frequently in temperate climates. Here amebic dysentery is comparatively rare and carcinoma is not frequent, while chronic severe colitis, mucous colitis, and achylia gastrica form the bulk of our patients. In office practice achylia and mucous colitis per-

haps rank first and second, while in hospitals the severe colitis forms are more frequent, for obvious reasons.

TREATMENT

The treatment may be divided into two parts: First, removing, as far as possible, all irritation from the intestines; second, combating the inflammatory process, and in the case of achylia and mucous colitis attacking the etiologic factor—*i. e.*, the absence of HCl, and the neurosis.

The removal of irritating factors, of course, depends on our opinion of the etiology of the disease. Taking the severe forms of colitis, for example, if we consider them due to sudden changes of temperature, the procedure is obvious. If due to specific infection, local or distant, then removal of the focus plus or minus vaccine treatment might be of benefit, but, as far as I have been able to ascertain, has not been so thus far. In such cases rest for the inflamed colon may be obtained in several ways—by complete rest in bed, by careful diet, and by surgical procedures. The first is essential, at least temporarily, in all severe cases, assisted by hot moist compresses.

As to diet, great difference of opinion reigns. Some with large experience believe that in large intestine inflammation of the type mentioned the chronicity is due to protein decomposition, and, therefore, advise elimination of all animal proteins. Others eliminate carbohydrates as far as possible, while others believe that patients do just as well with *no* dietary restrictions. In a disease like chronic colitis, which may have a relapse but once in one or two years, it is, of course, difficult to decide this matter, but in my own experience the kind of food is not nearly of so much importance as its preparation. The essential thing is that there be as little *coarse*, undigested residue in the large intestine as possible, and this can be easily attained by giving the diet thoroughly softened by cooking, and in a finely divided form, so that the cellulose of vegetables and connective tissue of animal food should be *minutely divided and softened*. The patient (in bed) is first placed for forty-eight hours on fluids, including tea, broth, gruels, cocoa, with water. Milk at first, and later should

be reduced to a minimum. This is a contradiction of what I stated above, viz., that the kind of food is not of first importance, but it has long been held, and I believe rightly so, that milk is an exception to this rule, and is contra-indicated in chronic diarrheas, and that it should be added late in the course of treatment, and then cautiously. I can give no explanation for this empiric fact. After forty-eight hours of such fluids we may begin adding special articles, and first the carbohydrates and fats, as fine white bread thoroughly toasted, butter, sugar, and gelatin. In two or three days more, squab or chicken may be added, and then the *finely divided* cereals, as cream of wheat or farina (with a small amount of cream and sugar) or tapioca. During this time two things are essential: First, the stools must be examined daily to see if undigested starches or fats are appearing in them. If so, then that particular variety of food must be temporarily eliminated. Here is where individualization is so important. And, second, we must maintain the general strength of the patient—*i. e.*, not allow him to emaciate. Those cases of chronic ulcerative colitis which have been reported as cured by removal of all dietary restrictions have, it seems to me, depended on this factor—viz., the improvement of the general condition by a more liberal diet and consequent increase in the ability to fight the secondary infections, which are the cause of the chronicity.

The third dietary period consists in the addition one by one, as in the second, and with the same precautions as to stool examinations, of eggs, light desserts, mashed potatoes, and vegetables which have been passed *through a hair sieve*. We generally begin with peas, tender carrots, and spinach. Later we may add scraped beef or other meats which have been passed through a fine meat chopper. This is in accord with the principle stated above, that the cellulose and connective tissue should be removed or finely comminuted, in order that they may be most easily attacked by gastric and intestinal juices, and that the residue may be as unirritating as possible.

As stated above, milk, plain, with lime-water, or in cream soups, is one of the latest to be added.

Such a diet will, in the majority of cases, cause a marked tem-

porary alleviation of symptoms, and while extremely monotonous, can be kept up for several weeks and extended, if symptoms permit, or further limited, if necessary.

One precaution must be observed, and that is the avoidance of constipation, so apt to occur after the acute exacerbation and often followed by an increase in mucus and blood in the stools. We may combat this complication by fruit juices early, and after the first three weeks of strict diet adding stewed fruit, straining out the coarser parts. Honey, levulose, and lactose are valuable, as is oil by mouth, straight or in emulsion with yolk of egg, sugar, and vanilla to conceal the taste. Petroleum oil may also be used. Later on, when the period of strict diet is over, agar-agar is sometimes useful, prepared in the same way and flavored as gelatin is.

Occasionally, when this type of diet fails we may try a cure of buttermilk or other type of fermented milk. It is at times successful, and this in spite of the fact that milk is ordinarily deleterious to a colitis patient.

In ulcerative colitis it would seem a rational procedure to use topical applications, as in chronic gonorrhea, and, in fact, the remedies recommended are legion, varying from the antiseptic astringents, as silver nitrate, through milder astringents, as tannic acid, to demulcents, like bismuth, and dermatol. I believe that the occasional success of such irritants as silver nitrate is far overbalanced by the number of cases in which the colon is finally irritated by their use.

At present I limit local application to one of four varieties: Hot normal salt irrigation, hot gelatin injections, bismuth emulsion, and occasionally tannic acid. The hot normal salt irrigation I believe is useful in the milder forms of colitis, as in mucous colitis. The water is allowed to run in through a rectal tube, and as soon as the patient experiences a sense of fulness the funnel is lowered and the water allowed to run out. Three or four quarts are used in this way, the treatment not to be repeated more than three times weekly, and stopped entirely if an increased irritation manifests itself.

The other irrigations can be used to advantage in the more severe forms. The gelatin is used in 10 to 20 per cent. solution at a temperature of 110° to 120° F., and 6 to 8 ounces allowed to run

in slowly and retained for a couple of hours. It may be preceded by a cleansing enema. The bismuth may be given in emulsion, beginning with ½-ounce to an 8-ounce mixture and tannic acid simply suspended in water in .03 to .05 per cent. solution. They should be retained a couple of hours at least and not repeated too often. I have seen no good effects from astringents by mouth in large intestine diarrhea. If all else fails, surgery may be employed. Probably the most successful is the appendicostomy procedure with, later, irrigations with the above-named substances. The objections are obvious. A remission occurs, though the appendicostomy is allowed to heal, and at the next exacerbation we are just where we were before. An artificial anus is much less permissible.

In mucous colitis the question of diet is even less settled. Many prefer the coarsest kind of foods, including coarse cereals, bran bread, coarse vegetables, salads, etc., but, inasmuch as spastic constipation is so often a part of the disturbance, a non-irritating diet described above seems to me more rational. The constipation can be treated as above, oil by mouth, oil enemas, and divided doses of cascara given in rotation, each for a period of a couple of weeks. Atropin by mouth is useful to relax the spasm. An easy way to give atropin is to begin with $\frac{1}{200}$-grain tablet twice daily, and increase one tablet each day until the physiologic symptoms are produced. It is not unusual to be able to give as high as $\frac{1}{25}$ or $\frac{1}{20}$ grain daily. We may keep up the course for three or four weeks, and after a rest repeat it.

Periods of irrigations with hot normal salt solution are of some value. In these cases, of course, psychotherapy must never be neglected, as it is not unusual to see an exacerbation follow every mental strain.

The achylia is finally, I believe, the ideal condition for the non-irritating gastro-intestinal diet outlined above, and responds to it almost invariably when sufficient HCl is added (at least 120 drops of the dilute preparation a day). It is rare that anything more is needed, though occasionally an astringent, such as tannalbin and bismuth, may be used for the first few days. When the food is delivered to the intestines in the proper condition for pancreatic digestion the diarrhea ceases.

CLINIC OF DR. M. MILTON PORTIS

COOK COUNTY HOSPITAL

SYPHILIS OF THE STOMACH

Rarity of the Lesion; Literature; Careful Interpretation Necessary.

Pathology.—Lesion of Tertiary Type; Gumma Most Common. Circumscribed: Ulcer, Pyloric Stenosis, Tumor. Diffuse: Cirrhosis.

Symptoms.—Variable, Simulating Ulcer, Stenosis, Carcinoma, Chronic Gastritis. Gastric Analysis: Non-obstructive and Obstructive Types.

Diagnosis.—History; Lesions in Other Organs; Bone, Liver, Skin, Nervous System; Serologic and *x*-Ray Findings.

Treatment.—Medical Treatment: Non-specific and Specific; Surgical for Mechanical Reasons.

May 16, 1916.

Present History.—This patient entered the hospital on October 28, 1915, complaining of pain in the epigastrium and splenic area. The present trouble dates back about nine years. The patient states that at that time she went to California on her wedding trip. While there she began to have a gnawing sensation in her stomach. Before this she was always healthy. This gnawing sensation did not occur regularly, had no relation to meals, and was not a distinct pain. She was not nauseated and did not vomit. This trouble was severe enough to bring her back to Chicago.

After returning, the patient was entirely free from pain until four years ago, when she began to have similar attacks. These have continued intermittently to the present time. On October 14, 1915, she suddenly experienced a sharp pain just below the left costal margin, which has been constant ever since. From

this time until October 28, 1915, she vomited four to six times, and this seemed to relieve the gnawing pain in the stomach.

On October 27, 1915, her condition became worse and the pain in the left side increased in severity. She was not nauseated, and without apparent cause vomited three bowls of blood. This seemed to relieve the stomach distress. The next day she came to the hospital, and it was noticed there that the stool was black and tarry.

Since leaving the hospital the patient has been up and doing her own work. The gnawing pain in the epigastrium stopped while she was in the hospital and was absent until about one week ago. At the present time the continuous pain in the left side is her chief complaint.

The bowels are constipated. She passes a considerable quantity of urine. Her appetite is good; in fact, she is always hungry. She has been careful about her diet, but this does not seem to affect the pain in the least. There is no shortness of breath and no edema. She has lost a good deal of weight, but does not know how much. She does not complain of lightning pains. She had some giddy sensations three or four times before coming to the hospital. There is no history of staggering in the dark. She has mild headaches occasionally.

Previous Illnesses.—She had whooping-cough and chicken-pox in childhood. Ten years ago she was sick for two weeks with typhoid fever. She never had rheumatism, sore throat, or pneumonia.

Family History.—Her father died of heart trouble; her mother died of a paralytic stroke; two sisters and one brother are living and well; there is no tuberculosis or cancer in the family.

Marital History.—The patient was married twice, first at the age of fifteen. During her first marriage she had one pregnancy. The child died in the third week of snuffles. Her husband left her after the first year. The second marriage took place in 1907 and there were no pregnancies.

Menstrual History.—She began to menstruate at the age of eleven; the menses have always been regular. During the past six months menstruation has been growing less, but is still regular.

Venereal History.—She denies venereal infections.

Habits.—The patient takes beer at her meals; for the past three or four years she has been taking whisky several times each day up to six months ago. She does not use any drugs.

Physical Examination.—The patient lies comfortably in bed and is able to move about and sit up. She is somewhat emaciated; she does not complain of any pain at present. The pulse is 95, temperature 99° F., and respirations 24.

Head and Neck.—The scalp is negative. There is no edema of the lids. The pupils are slightly irregular, the right a little larger than the left. Reaction to light is sluggish; both react to accommodation promptly. The nose and ears are negative.

The lips show pallor. Many of the teeth are decayed and pyorrhea is present. The tongue is coated, but does not show any scars. The tonsils are small.

Examination of the Chest.—The lungs are negative. The heart borders are normal; the tones are clear, without any murmurs. The blood-pressure measures 142 systolic and 99 diastolic, giving a pulse pressure of 43.

The superficial vessels are somewhat thickened.

The *abdomen* is flat, not distended and not rigid. There is some resistance in the epigastrium and tenderness is noted here. The lower border of the stomach extends several inches below the umbilicus. The *liver* and *spleen* are not palpable.

Examination of the *genitalia* does not show any evidences of syphilis, but does show a laceration of the perineum and cervix of the uterus. The uterus is freely movable and the adnexa are negative.

The patient has external hemorrhoids, but there is no stricture or other trouble in the rectum.

The *knee-jerks* are absent, even with reinforcement. The patient shows a positive Romberg. There is no Babinski and no clonus is present in the ankle or patella.

The *skin* does not show any scars suggestive of syphilis.

The Temperature-curve.—Since the patient has been in the hospital she has not at any time shown any increased temperature except for an occasional rise of 1 degree. The respiration and

pulse-rate have both been normal, and under proper diet and medication she has been comfortable and is becoming more so constantly.

The *urine* does not show any abnormal findings.

The *blood* shows the picture of a secondary anemia. The hemoglobin has varied from 35 to 55, the red counts between 3,000,000 and 4,000,000, and the leukocytes around 10,000, with a slight increase in the polymorphonuclears. The blood shows *a strongly positive Wassermann*. The spinal fluid shows a cell count of 72 and a strongly positive Wassermann.

Frequent *stomach tests* have been made. There is delay in the emptying time of the stomach, sometimes two or three hours beyond the normal. Analyses of the stomach contents have shown an average of 25 free and 65 total acid. Blood has been present chemically most of the time. The stools likewise have shown the presence of occult blood until the past month, when repeated stool examinations have not shown any occult blood.

The *x-ray examination* made by the resident röntgenologist, Dr. Blaine, shows (April 13th) a large size six-hour residue. The second meal reveals an hour-glass stomach. The constriction is located in the pars media. The defect is smooth in outline. Opposite the contraction on the lesser curvature an outcropping is seen similar to that seen in a perforating ulcer. The first, second, and third parts of the duodenum are greatly distended.

A repetition of the examination (May 12th) shows similar findings to those described. There is still a motor insufficiency, but the constriction seems less marked and the lesion appears decreased in size.

I have given you a schematic outline so that we can cover the subject of syphilis of the stomach in a more logical manner. In the first place, the diagnosis of syphilis of the stomach is only made at rare intervals and it is undoubtedly a rare condition. The entire medical literature probably does not cover 100 cases. The largest group of cases has recently been reported by Eusterman, of the Mayo clinic. He reports 23 cases. Lewald, of New York, has described 5 cases with *x*-ray findings, and points out what he considers some characteristic evidences.

O. Clark has recently reported 11 cases. It is more than likely that the cases are more common, but are not often recognized. Many patients with active syphilis have gastric symptoms, and we are apt to conclude that these are produced by the medication, or are of reflex origin. We must be careful how we interpret gastric symptoms in luetic patients. It is very possible that an

Fig. 54.—Hour-glass stomach with deformity. Probable syphilitic ulcer basis (Blaine).

individual with ulcer of the stomach may acquire lues, and vice versa. There is no reason why a person who has had lues should not acquire a gastric ulcer. Carcinoma may occur in individuals with syphilis and may have no direct relation to the previous syphilitic infection.

In the treatment of syphilitic cases, especially where large

amounts of the iodids are given, many individuals have gastric symptoms, and hence it is possible that cases with chronic gastritis may be interpreted as syphilis of the stomach.

Antisyphilitic treatment may exert a favorable influence on any pathologic process in a syphilitic individual by improving

Fig. 55.—Gastric syphilis. Contraction of lower half of stomach into narrowed channel (Case).

the general health. Hence the cure or improvement of non-specific stomach disease by such medication is no proof of the presence of syphilis of the stomach. So one should be very careful of the interpretation of gastric symptoms in cases that have a definite clinical picture of syphilis.

Pathology. There is no doubt that all of the various pathologic lesions of syphilis can occur in the stomach, the secondary manifestations as well as the tertiary, but most of the cases described in the literature have pathologic findings of the tertiary type—the gumma. Gummata have been described in the submucosa in the earlier cases. From this localized or circumscribed invasion of the submucosa with the gummatous lesion a variable

Fig. 56.—Extensive filling defect simulating gastric syphilis. Tissue section showed carcinoma of stomach (Case).

group of pathologic findings can arise. For example, multiple gummata may coalesce into a large lesion and form a tumor mass resembling carcinoma. Healing of the gumma with scar-tissue formation may result, or it may break down in the central part and break through the outer portion, producing an ulcer or perforation. Then, again, we may find an invasion of the entire stomach wall by a low-grade syphilitic process with over-

growth of connective tissue simulating a cirrhosis of the stomach. It is possible that the small stomach found in some cases of chronic gastritis may be of syphilitic origin and may belong to this group.

The circumscribed cases are apt to give the pathologic picture that we find in ulcer of the stomach, and this ulcer may look very much like a peptic ulcer. On the other hand, with healing and contraction of the scar tissue in the region of the pylorus, the pathologic picture may be that found in pyloric stenosis, and it may simulate a non-specific pyloric obstruction. In other cases a massing or grouping of the gummata produces an actual tumor which may be palpable. These are the cases that are mistaken for gastric carcinoma. They are at times difficult to differentiate until very careful microscopic and histologic studies are made to show the definite syphilitic pathology, particularly the characteristic giant cells, or until the spirochete itself is demonstrated in the lesion. At times the surgeon or pathologist is not able to decide from the gross specimen whether or not there is carcinoma or syphilis, and I want to emphasize this point because it is of great clinical value.

The blood-vessels frequently show endarteritis. The diminished blood-supply may account, on the one hand, for the degenerative changes with connective-tissue overgrowth, while, on the other hand, if the blood-supply is diminished in localized areas ulcers may result from the digestion of the anemic areas by the gastric juice.

Symptoms.—The symptoms of the disease are not characteristic. The clinical picture is a variable one and it depends upon the pathologic changes that are present. The picture may simulate ulcer closely, and a number of the cases described by Esterman were cases that would pass for ordinary gastric ulcer with pain, nausea, vomiting, and hemorrhage. There are also cases with syphilitic pyloric stenosis which simulate pyloric stenosis that is not of specific origin. Again, there are cases that resemble carcinoma very closely, with all the signs and symptoms, including a palpable tumor. Lastly, a group which resembles chronic gastritis has been described.

The *gastric analysis* in cases of syphilis of the stomach is again a variable one. A large majority of Eusterman's cases showed marked reduction of hydrochloric acid, and most of them showed complete absence of free hydrochloric acid.

The gastric analysis in cases without pyloric obstruction shows subacidity or anacidity, but when obstruction is present with motor insufficiency, then lactic acid is found, and the findings resemble very closely those of cancer of the stomach. Oppler-Boas bacilli have been described and usually there is blood present. In a few of the cases, 2 of which are reported by Einhorn, free hydrochloric acid was found. But remember that the majority of cases show markedly reduced acid or absence of acid. In a number of cases mucus was found in excessive quantities, as occurs in chronic gastritis.

Diagnosis.—In the diagnosis of the condition a history of an acquired infection, or one of congenital origin, is of great value. In the 23 cases which Eusterman described only one-half gave a definite history of syphilis, so that in spite of a negative history you may still have syphilis of the stomach.

You will be further aided in the diagnosis by a recognition of syphilitic disease elsewhere in the patient. Look especially for bone lesions, particularly tibial periostitis and skin lesions. The thin, papery, brownish pigmented scars are the type of skin lesions most commonly found in late syphilis.

Look also for visceral lesions, especially syphilis of the liver. An enlarged nodular liver with hepatic fever is frequently of syphilitic origin. Finally, examine for lesions of the nervous system which we associate with syphilis.

The patient shown today has findings that we can classify as tabes dorsalis, which we know in practically all cases is of syphilitic origin.

So the finding of syphilitic lesions in other parts of the body is of great value in helping you to decide whether the stomach lesion may or may not be of syphilitic origin.

The newer work in the diagnosis of syphilis involves the *serologic tests*. The Wassermann test is of great value when positive. A number of the cases that Eusterman described did

not give a positive Wassermann test, either in the blood or in the spinal fluid, even when a provocative injection of salvarsan was given.

When the Wassermann test on the blood is negative it is best to make a Wassermann test on the spinal fluid. At the same time examine also for the cell count which is generally increased in syphilis and may be 50 or more, and the Lange Gold test, which, in the hands of careful workers, gives definite evidence of syphilis.

The *x-ray findings* in syphilis of the stomach show nothing pathognomonic. There is no definite *x*-ray evidence which would lead one to make the unqualified diagnosis of syphilis of the stomach. Lewald divides the *x*-ray findings in three groups. In the first group he describes a small stomach, with an infiltration in the pars media, producing a dumbbell-like appearance in the stomach, somewhat similar to the one we showed this morning, but not presenting the lesion on the lesser curvature which this patient had. It is an exaggerated hour-glass, looking more like a dumbbell. In these cases with small stomach there is usually some compensatory dilatation of the esophagus. In the next group he describes cases with pyloric obstruction and dilatation, and in the third group he describes cases which have *x*-ray findings of chronic ulcer, with hour-glass stomachs and defects in the shadow similar to that seen in cancer of the stomach.

So when we sum up the evidence, the *x*-ray findings look like any one of the conditions we have described in the clinical picture. Possibly the dumbbell appearance described by Lewald and the *x*-ray findings described by Case (Fig. 55), which is a contraction of the pyloric half of the stomach due to an extensive cirrhotic change, may be characteristic of syphilis. The *x*-ray has a place in the diagnosis, but it should be combined with the other findings described.

Figures 57–61 are from the Röntgen department of the Mayo clinic, and illustrate cases described by Eusterman.

Treatment of Syphilis of the Stomach. It is best to consider the treatment of syphilis of the stomach from two angles. The treatment that you would ordinarily give, medical or surgi-

cal, for the non-specific condition that you think is present, and, second, to combine with it specific treatment. If the patient presents a lesion that does not have any suggestion of carcinoma

Fig. 57.—Gastric syphilis. High hour-glass; upper loculus only visualized. Retention of one-fourth the six-hour meal (Carman).

and the clinical picture warrants carrying out medical treatment, I think it is wise first to combine with the medical treatment active specific therapy, and watch the case for several weeks or

months before definitely deciding to institute surgical procedures. If, on the other hand, the patient shows anything at all suspicious of cancer, and I emphasize that because that is the condition which will come up, I do not feel that we are wise in delaying operative

Fig. 58.—Gastric syphilis. Hour-glass stomach with irregularity at *A*, corresponding to palpable mass. Retention of one-fourth the six-hour meal. Reflux of the meal into the esophagus (Carman).

interference. I do not think that the clinical picture or the findings of the type I have described are diagnostic enough to say that it is not a cancer, nor have we in cancer of the stomach enough definite evidence to be able to say, "Yes, this is surely a cancer or is not a cancer." Therefore, if there is any suspicion

in the sum total of the evidence of the case that it may be an early cancer, advise surgical intervention at once, whether the patient has or has not specific findings elsewhere.

Even if at the time of operation evidences against carcinoma are found, it is advisable to remove the tumor mass, for such areas may cause mechanical disturbances later on which would necessitate surgical aid.

Fig. 59.—Gastric syphilis. High hour-glass, with marked narrowing and deformity in the body of stomach (Carman).

In the cases where surgical treatment is not indicated at once it is best to start a thorough medical course of treatment for the condition and combine with it active specific treatment. The active specific treatment involves not only the old method of treatment by mercury and iodids, but the newer treatment with salvarsan. The salvarsan should be given vigorously. In

my own practice I start out with a small dose, $\frac{3}{10}$ gram, for the first injection, then gradually work up to the maximum dose of $\frac{6}{10}$ gram of the old salvarsan and give this intravenously. I never give less than six injections of salvarsan at intervals of one injection every week or ten days. The salvarsan may also be given intramuscularly. In the interval between the salvarsan injections and following the last injection the patient receives

Fig. 60.—Gastric syphilis with marked irregularity of body of stomach. No retention from the six-hour meal (Carman).

active mercurial treatment. This may be inunctions of mercurial ointment or, better still, injections of mercurial preparations. A thorough course of mercurial treatment should be carried out in addition to the salvarsan, and I think it wise to give the patient after the course of mercury, or at times during the mercurial treatment, large doses of potassium iodid. If this therapy is not well tolerated by the stomach it can be omitted, but oftentimes

large doses of iodids given an hour after meals in carbonated liquids will be well borne.

The medical treatment of the patient we presented today is that of ulcer of the stomach. I feel that we have definite clinical, laboratory, and *x*-ray evidence for gastric ulcer of the perforating

Fig. 61.—Gastric syphilis. Large stomach. Retention of half the six-hour meal. Filling defect at pyloric end, *A* (Carman).

type, whether of specific or non-specific origin. There is no evidence in the *x*-ray examination or in the laboratory findings to speak for carcinoma. In the course of the treatment the patient has improved clinically. The *x*-ray evidence also shows improvement. So I think we are justified in continuing the treatment we are carrying on, but if in the course of the next

month or two the patient shows any acute symptoms, or shows more marked obstruction, or shows a menacing hemorrhage or repeated small hemorrhages, I would insist upon surgical treatment.

The medical treatment of ulcer of the stomach I will not consider in detail at the present time, but I will say, in brief, that it consists of feeding the patient every two hours with milk and cream, eggs, and soft vegetables, followed by alkaline therapy. This patient has, in addition, treatment for her anemia and has had active specific therapy. Her teeth should be radically treated, and all root infections removed by extracting the teeth.

Even though you feel that the gastric lesion is not of syphilitic origin, if the patient has other evidences of syphilis it is wise to give antisyphilitic treatment in addition because of its tonic effect. Besides, remembering the endarteritis which is common in syphilis, you may improve the arterial blood-supply to the part that is under treatment.

In closing, permit me to emphasize one point more. Every case of inoperable cancer of the stomach, even though you cannot find any definite clinical evidence of syphilis, or anything at all that points to the diagnosis of syphilis, should receive the benefit of the doubt at your hands and have an active course of syphilitic treatment. I think that it is a wise thing to do, because in a small group of cases you will get clinical improvement which, of course, would not occur without such treatment. I have one case in mind that was on my service a few months ago. A young colored boy, about twenty years of age, had a definite clinical picture of lues, but the *x*-ray evidence and the laboratory findings pointed toward the diagnosis of cancer of the stomach. I felt that we did not dare put him through the usual medical treatment of syphilis along with treatment for his stomach condition, but sent him to the surgical department. He was operated upon by Dr. Dyas, who, when he opened up the abdomen, said it was an inoperable cancer, and referred him back to the medical department. I put him on specific treatment, and the patient began to improve in weight and in his general condition. He left the service feeling very much better. Later he reported that he was decidedly improved.

CLINIC OF DR. CHARLES LOUIS MIX

MERCY HOSPITAL

PLEURISY AND GASTRIC SPASM: THE MORPHIN HABIT SUBSEQUENT TO LEAD COLIC

Special Reference to the Use of Belladonna as a Therapeutic Agent in Gastric Spasm.

April 4, 1916.

THIS patient entered Mercy Hospital on March 9th with the following history: He is forty years old, by occupation a printer. His father died at eighty-six years, of old age; his mother is living and well at eighty. He has a brother and sister living and well. There is no family history of tuberculosis or carcinoma. He is married and has two healthy children.

Past History.—He had chicken-pox when a child and was jaundiced at eighteen. At this time his hair fell out, but afterward grew in again. He was sick for two months, but had no fever. He came to America and started to work as a printer about fifteen years ago. Shortly after that he had what he calls "printers' colic," associated with a great deal of abdominal pain.

DR. MIX (to Patient): When you had printers' colic were you setting type by hand?

PATIENT: Yes, in a job office.

DR. MIX: Linotype men do not get printers' colic because they use a machine and do not touch type, but job printers get printers' colic frequently because they handle the metal type.

His present trouble began Sunday, March 5th, with pain in the limbs, headache, and a feeling of nervousness. He went to work on Monday, but was sent home on account of pain in the right side of his chest and headache. He began to cough

that night and the pain grew more severe, especially on deep breathing. He evidently had a classic case of pleurisy with signs of general infection; the pain was especially severe and sticking in character on deep breathing. He called a physician, who said he had pleurisy and a high fever. The following day he raised a brownish-red sputum, and the doctor then said he had pneumonia. On Wednesday night he started to vomit a deep-greenish material. He could keep nothing on his stomach and had cramp-like pains. He was brought to the hospital four days after the beginning of his illness.

Examination of the feces, made because of the persistent vomiting, though associated with little or no nausea, showed no blood. A blood-count revealed 11,600 leukocytes, 3,850,000 reds, hemoglobin 70 per cent., blood-pressure 114. A differential white count showed a lymphocytosis and a diminution of the polymorphonuclear cells instead of the usual polymorphonuclear leukocytosis of an ordinary case of pneumonia. The blood-count is rather what one might find in some cases of inflammation of the pleura. A later examination of the blood, made March 27th, showed a leukocyte count of 6200, 3,920,000 reds, hemoglobin 70 per cent.

The temperature on entrance was 100.3° F.; the following day it fell to normal notwithstanding the fact that he had a great deal of pain in his side. It has remained normal ever since.

Examination of the sputum showed staphylococci and streptococci, but no tubercle bacilli. Examination of the urine showed some albumin present, a slightly alkaline reaction, but nothing further than that. This examination was made on the 10th. On the 11th the urine showed a few hyaline casts. Since then there have been no abnormal findings.

Physical examination showed, upon entrance, the usual signs of a plastic pleurisy, with a friction rub. There were no signs of pneumonia. He was treated with sodium salicylate and rapidly recovered from his pleurisy.

Now, there are other features of his case which are the reason for his being here this morning. The history which the intern wrote was incomplete, so that we shall have to amplify it somewhat as

we go along. In the first place, you will notice on his abdomen dilated capillaries and a scar at this point, but there is nothing in the intern's history about these findings. (To Patient): When was the first time you ever had trouble with your abdomen?

PATIENT: About ten years ago.

DR. MIX: What was the trouble at that time?

PATIENT: I had very hard cramps. One evening when I was going out I was taken with very severe cramps which threw me down on the floor.

DR. MIX: Did you have any fever at that time?

PATIENT: Not that I know of.

DR. MIX: Did you vomit?

PATIENT: Yes.

DR. MIX: Were you constipated or did your bowels move?

PATIENT: I was badly constipated, but they moved.

DR. MIX: How long after you had been setting type by hand was it that you had these severe cramps or colic?

PATIENT: About three years.

DR. MIX: So, after three years of type-setting he suddenly had a severe abdominal colic associated with notable constipation. Such a history in a type-setter, working with lead type, raises the presumption of but one possible diagnosis, and that is, lead-poisoning. Please note the symptoms. The bowels moved, but there was colic. It was not a case of bowels not moving at all in the presence of colic. In the latter event we might suppose a blockade of the bowel, absolutely preventing the passage of feces, with tremendously painful peristaltic waves vainly endeavoring to sweep fecal matter past the obstruction, thus leading to intolerable colicky pain. Such a set of symptoms results from obstruction from bands of adhesion, from Meckel's diverticulum, from invagination, or obturator ileus. And in time reversed peristaltic waves would occur in an endeavor to free the intestines from their contents: and vomiting would result—persistent, foul, and ultimately fecal—just before it is time to send for the undertaker.

On the contrary, in this case the bowels moved, but they moved only with urging. There was the presence of severe, col-

icky pains, but no vomiting. Such a set of symptoms is highly suggestive of lead-colic, a hypertonicity of the small intestine and colon. The lead causes a spasticity of the bowel which is painful to a degree, but there is no reversed peristaltic wave and no fecal vomiting.

Hence it is that morphin and opium, which ordinarily cause marked constipation, by stopping peristalsis in cases of severe constipation from lead-poisoning, relieve the constipation. They do so by lessening the peristaltic spasm. The spasm being stopped by the morphin or opium, the bowels once more begin to move.

(To Patient): How long did this attack last?

PATIENT: Two weeks; the doctor gave me laudanum.

DR. MIX: And that cured you?

PATIENT: Yes.

DR. MIX: This is now a perfect history of lead-poisoning and lead-colic. We have the story of a patient handling lead type, getting an abdominal colic with marked constipation but no obstipation, and being cured by laudanum. (To Patient): What was the next thing?

PATIENT: I was well about a year, and then it came back again.

DR. MIX: How long did the second attack last?

PATIENT: About three weeks; it was worse than the first one.

DR. MIX: When did you get the wrist-drop?

PATIENT: The last time.

DR. MIX: I asked this question because you will *never* see a case of wrist-drop from lead-poisoning until there has been at least one attack of lead-colic. In other words, you have to have enough of the constitutional effect of lead upon the body to produce at least one attack of colic before you get enough effect upon the nerves to produce sufficient degeneration to cause wrist-drop. The wrist-drop is *always* bilateral because the lead is circulating in the blood. It affects the musculospiral nerves of both sides and, therefore, the patients have double wrist-drop. Pressure on one musculospiral nerve in the stupor of drunken sleep produces unilateral wrist-drop. Bilateral wrist-drop is due to constitutional and not to local causes. The second attack was more

severe and lasted three weeks. (To Patient): What was the next thing?

PATIENT: The attacks came on oftener; the next one was in ten months, and then oftener and oftener.

DR. MIX: All this time you were doing the same kind of work?

PATIENT: Yes, but I don't set type by hand very much now.

DR. MIX: But the attacks came on more and more frequently. When were you operated upon?

PATIENT: Eight years ago.

DR. MIX: Why were you operated upon?

PATIENT: I don't know.

DR. MIX: What were your symptoms?

PATIENT: The same as now.

DR. MIX: Did the operation cure your condition?

PATIENT: No, I stayed much the same.

DR. MIX (examining abdomen): What is this little scar here?

PATIENT: That was an abscess from a hypodermic injection.

DR. MIX: Do you know what was done at the time of the operation?

PATIENT: They told me they took out the appendix, but it did not stop the colic.

DR. MIX: Was there any tenderness?

PATIENT: No, it felt crampy, but pressing on it relieved the pain.

DR. MIX: Note well the patient's answer. *Pressing on it relieved the pain.* Is that true of pressure over a diseased appendix? In an ordinary colic due to spasm the pain is relieved by pressure, but in pain from an infected gall-bladder, a diseased appendix, or a duodenal ulcer pressure makes the pain worse rather than better. It is hard to see why an operation was done in his case, but I am of the opinion that it was done as an exploratory measure. Doubtless there was not a typical lead-line and a genuine lead-colic was not regarded as a likely diagnosis. Yet one must frequently make a diagnosis on the evidence of symptoms alone, and one must stick to the clinical story because it usually carries with it the exact diagnosis. A carefully written history affords 75 per cent. of our data in most abdominal cases.

Out of this lead-colic there has arisen a rather bad thing for the patient, and that is a gradually increasing tendency to take morphin, opium, and laudanum, so that when he came into the hospital we had a terrible time with him. He is very grateful to us now for having stopped his habit. He is very greatly improved and feels much better, having been forced against his will to the stopping of his morphin, for which he at first most bitterly begged. "Nur einmal" (only once) he used to beg of me. A person who has attacks of colic which are easily relieved by opiates acquires a tendency toward their use, and this tendency soon becomes an overpowering habit. Then the abstraction of the drug often produces a pain which is honestly mistaken for the original pain, so that both patient and physician may be deceived. I think that this is what happened to him. After he had been relieved for a certain time by hypodermic injections the lead-colic pains entirely ceased, but the abstraction pains were substituted for them, so that he demanded morphin really because of abstraction pains and not because of the colic. These patients cannot reason out their pains, and they do not know that they have to suffer severe abstraction pains before they are relieved of their morphin habit. This man did not have a very bad habit because we have already broken him of it completely. When he first came into the hospital he made life miserable for everybody around him by begging persistently for hypodermic injections, but now he does not want them.

The pleurisy and the morphin habit being disposed of, a third part of his case, having to do with his stomach and stomach findings, remains for our further consideration. After we had gotten rid of the worst of his symptoms caused by the morphin habit, we turned our attention to his vomiting. We found that about half an hour after he ate his meal everything came up. This went on day after day with a great deal of regularity. As soon as he would take anything into his stomach a very active peristalsis began, with very rapid emptying. Examination of the stomach contents showed on March 13th no free hydrochloric acid and a total acidity of 17. The vomiting persisted continuously from the beginning of his stay with us. There was no lactic

acid and no blood in either vomitus or stomach contents. An examination of the latter on the 20th showed free hydrochloric of 8, no lactic acid, and no blood.

His is a case of gastric spasm, with hyperperistalsis, low acidity, and vomiting by regurgitation. A good many similar cases are reported in the medical literature. In the last few years duodenal and gastric ulcer have crowded out from the minds of many men all thoughts of other gastric ills. But by use of the *x*-ray and by fluoroscopic examination it has been found that there are many kinds of gastric neuroses. These are usually due to previous disease or to adhesions, frequently to some old disease of the appendix or duodenum. Sometimes, however, we can't find any evidence of such disease. For example, in this case the only thing we could find in his history was the jaundice in his eighteenth year associated with alopecia. There is nothing else in the history except the printers' colic and the morphin habit, which is apparently cured at present. But there remains the condition of vomiting all of his meals.

(To Patient): How long has it been since you vomited?

PATIENT: Not since I got the new medicine.

DR. MIX: The "new medicine" was something that controls spasm of the stomach, and that is tincture of belladonna in 10-drop doses before each meal. It should be given long enough before the meal to make certain that the full physiologic effect may be brought out by the time the meal is eaten. There are many individuals who are so nervous that it is impossible to tell a thing about the condition of the stomach by fluoroscopic examination or the making of skiagrams because of this marked peristalsis. In many cases a perfectly simulated hour-glass constriction of the stomach will be found in the skiagram, and a surgeon will operate with great assurance of the correctness of his diagnosis, and yet nothing will be found. After a multitude of such experiences it was apparent that such cases are really due to an exaggerated peristalsis upon a nervous or neurotic basis. Hence the practice began of giving to such patients tincture of belladonna in full physiologic doses so that spasm might be overcome before the skiagram was taken.

In a case like that with which we are dealing, if the spasm shuts the pylorus there is nothing for the food to do in cases of exaggerated peristalsis but to come up. If the pylorus is not closed by spasm there is a very rapid emptying of the stomach contents into the duodenum by the exaggerated peristalsis. We must assume in this case pyloric closure, with simultaneous exaggeration of peristalsis, which leads to the regurgitation of the patient's food; and we are the more willing to adopt this assumption because in this case the regurgitation is not attended with nausea, thus strongly suggesting the neurotic element in his case. Of course such a condition is very burdensome to a patient, and has been so to him. Whether the neurosis is in any way associated with his morphin habit I do not know. It is not unlikely that his nervous instability is largely due to this terrible addiction.

I believe that at the beginning this patient had a common, ordinary case of printers' colic due to lead-poisoning from the handling of type metal, and that he was cured by laudanum, but that subsequently, by abandoning job-work type-setting and by adopting the use of a linotype machine, further poisoning by lead ceased. This is likely because he has had but one attack of wrist-drop, which took place several years ago. I believe further that the pain of the lead-colic led to the acquisition of the morphin habit, and that a time came when the patient confused his abstraction pains with the pains which he used to have as a result of his lead-colic. Then subsequently the gastric neurosis developed, with continuous regurgitation and vomiting of food after each meal, but associated with no nausea. Thus it came about that he lost about 25 pounds in the last two years, not altogether because of his morphin habit, but because of the regurgitation and vomiting. Since the latter has been controlled by the belladonna he has gained 7 pounds in the last ten days, because he no longer regurgitates meals within half an hour after they are eaten. We expect to keep him in the hospital a little longer until his weight is still further increased.

This is a very interesting case, though he entered the hospital merely for an attack of ordinary pleurisy. If we had stopped with that diagnosis and the cure of that acute infection, if we had lost

courage in the face of the morphin habit, we would not have gone as far with our patient as our duty to him demanded of us. This case emphasizes the importance of our social as well as of our professional obligations. This man, now that he is cured, realizes that he has been the victim of a drug habit, and he is never going to take any morphin or opium again. The case also proves the contention of radiographers that there are many cases of gastric spasm which lead to vomiting and regurgitation without nausea, the regurgitation being upon purely a nervous basis. Such patients are readily helped, as was this one, by the administration of belladonna in full physiologic doses.

NOTE.—The patient subsequently left the hospital several pounds heavier and entirely cured of his pleurisy, morphin habit, and gastric spasm. He remained about six weeks after his case was clinically demonstrated, and the morphin craving had entirely disappeared.

A CASE OF MYELOGENOUS LEUKEMIA

January 31, 1916.

THIS gentleman is a private patient of Dr. J. B. Murphy, whom I examined at his request. He is twenty-five years of age, married. He entered the hospital on account of pain and tenderness in the right side, intermittent fever, and nausea. He had the usual diseases of childhood; diphtheria at sixteen, without complications. A brother is said to have died of heart disease at sixteen years of age. On cross examination it seems possible that this brother had tuberculosis. There is no history of carcinoma in the family and no venereal history. His wife has had one miscarriage; she has no living children. The patient twice had malaria four years ago in Cuba. The first time he was sick for about two weeks and the second time he was sick a still shorter time. There was only a short interval between these two attacks, so that the second was undoubtedly a recurrent attack following the first infection.

DR. MIX: Did you have pain in the right side when you entered the hospital?

PATIENT: Yes, on both sides and in the stomach.

DR. MIX: The patient has had pain in the epigastrium and abdomen after meals for the last year. This pain was accompanied by gas formation in the epigastrium with eructations of gas and a sour taste in the mouth. Food aggravated the pain; sodium bicarbonate relieved the gas. He has never vomited. He has been tender to pressure in the epigastrium for about a year. The attacks of pain occurred at intervals for one or two weeks and he would then be free for two or three months. The bowels are constipated; he has never passed blood or mucus.

On Christmas day the patient had a sharp cramp-like pain in the lower left side which doubled him up. It lasted only a few moments each time, but repeated itself every day for about

a month. During this time he noticed that on stooping over he would get dizzy, black spots would appear before his eyes, and he would grow faint. He noticed no mass in the abdomen. There has been nothing wrong with the joints, no nausea or vomiting, chills or fever. During this period his energy seemed to wane and he could not perform his usual amount of work. His hearing seemed to be decreasing. His wife noticed that he did not grasp questions with his usual quickness and that his memory was poor. About this time he developed a dry, brassy cough. He had no hemoptysis, but he lost a great deal of weight. He gradually grew weaker, and the pain in the left lower quadrant of his abdomen continued until January 10th, when he had a sharp pain in the right lower quadrant. He was walking on the street at the time, and stopped and pressed his knee up against the abdomen and that relieved the pain. At that time he had some fever, but did not vomit, although he felt nauseated. The pain lasted about one-half hour and then disappeared, leaving a feeling of tenderness over the right iliac fossa. For the last seven nights he has wakened from sleep drenched in sweat. There has been a gradually increasing pallor. He has noticed no change in the genito-urinary apparatus. He has had two other attacks of pain since the attack mentioned. He has never been jaundiced. His eyes react to light and accommodation and the knee-jerks are present.

We have here a history which is rather complex and rather difficult at first sight to harmonize with a clinical entity. When he entered the hospital he had a set of symptoms which were largely abdominal, and which might at first glance seem to be due to disease of the stomach, duodenum, or gall-bladder. Indeed, as he has told the story, one might well base upon it the diagnosis of a cholecystitis, because there was tenderness over the right costal border in the region of the gall-bladder. The whole story is suggestive of cholecystitis. It began with a series of digestive disturbances resembling those of cholecystitis, consisting of the belching of gas, spells of indigestion, and attacks of severe pain in the right hypochondrium. One of these attacks was a typical colicky attack, occurring suddenly upon the street,

and being relieved by the pressure of his knee upon his abdomen. Though at first there was neither nausea nor vomiting, nausea later became a symptom. Moreover, the malady was characterized by a series of attacks, just such periodic seizures as occur in cholecystitis and cholelithiasis. There are, however, many other points in the story which do not confirm the diagnosis of biliary tract infection. These are chiefly the symptoms associated with severe anemia, consisting of a gradually increasing pallor, a marked degree of increasing asthenia, attacks of vertigo upon stooping, deafness, and possibly the inability to grasp questions with his former quickness, together with an impairment of memory. Important, too, in any case in which the diagnosis of cholecystitis is contemplated is the absence of signs of infection, of joint disturbances, chills, or fever. True it is that of late there has been fever with night-sweats, but these are a very late development. Taking all the symptoms into consideration, having in mind also the possibility that the malaria in Cuba might figure as an etiologic factor in biliary tract infection, we are forced to confess that we can neither affirm nor deny the existence or absence of cholecystitis or cholelithiasis. Though we feel that, on the whole, the arguments in favor of cholelithiasis outweigh the arguments against its presence, it is still evident that something more vital must be affecting the patient's strength and vitality.

Has the patient an ulcer of the stomach? The indigestion, gas, and belching which ushered in his symptoms one year ago were quickly followed by the aggravation of these symptoms by the taking of food. Moreover, there is a strong hint of hyperacidity, both in the sour taste in the mouth after belching and in the relief afforded by bicarbonate of soda. Very characteristic, too, is the epigastric pain (apart from the attacks of abdominal pain) and the late nausea. Epigastric tenderness raises further suspicions, confirmed by the presence of constipation, so common in ulcer both of the stomach and duodenum. His very age, twenty-five years, an argument militating mildly against the diagnosis of a biliary tract infection, tends to support a diagnosis of ulcus ventriculi. The loss of weight, the absence of signs of joint in-

fections, of chills, fever, and sweats in the first year of his illness, together with the periodicity of the seizures, arouses keen suspicion as to ulcer. The increasing pallor might have been produced by hemorrhage from such an ulcer, but there is no history of melena or of hemorrhage from the mouth such as occurs in ulcer associated with pallor. In ulcer pallor is of sudden onset from large hemorrhages. It is never of gradual onset from oozing of blood from an ulcer, because ulcers do not ooze; they bleed hard or they do not bleed at all, and pallor in ulcer is of sudden and not of gradual onset.

On the other hand, a diagnosis of ulcus ventriculi does not at all explain the attacks of severe abdominal pain. These best conform with the diagnosis of cholelithiasis. There is too much pain in the right left and the right lower quadrant of the abdomen, as well as in the right upper quadrant. The asthenia is not properly accounted for in such a diagnosis, and the late mental changes, the late fever, the drenching night-sweats, and the dark spots before the eyes upon stooping are left unexplained.

Could he have an ulcer of the duodenum? This is very unlikely, because the story of his symptoms scarcely resembles the story of ulcer of the duodenum at all. The well-known relation between food and pain obtaining in this condition is absent. Pain does not come on one or two hours after meals, and is not relieved by the further ingestion of food. The pain is too severe, it is too paroxysmal, and it is associated with nausea. Indeed, so little characteristic is the story of duodenal ulcer that the probability of such an ulcer being present is exceedingly slender.

One might entertain the diagnosis of appendicitis in his case because of the attack of pain on one occasion in the right iliac fossa, this pain being associated possibly with fever at times, though we cannot be certain as to this point. But this pain was relieved by the patient's pressing his knee hard against his body, thus indicating its colicky nature, a colicky pain being so relieved; and at the same time indicating that it was not caused by appendicitis, because the pain of appendicitis would be immensely increased by such pressure. Moreover, appendicitis usually

begins not paroxysmally, like strangulated hernia or perforated ulcer, but gradually, with diffuse pain all over the abdomen. This is followed by one or two attacks of vomiting and then vomiting ceases. In a few hours more, twelve to eighteen, the pain localizes in the right iliac fossa. Meanwhile the temperature rises slightly in 999 cases out of 1000. A white count, too, always shows a leukocytosis. In this patient's case an entirely different story is met with. Surely, on thought, there can be little possibility that either a duodenal ulcer or appendicitis is present. Of gastric ulcer there may be a possibility, but of cholelithiasis and cholecystitis there is a probability.

There is a most important symptom mentioned prominently in the case because it is prominent in the patient's mind, and that is bodily weakness. He complains of a degree of asthenia which is never found in either infections of the biliary tracts or of gastric ulcer. He complains of waking up at night of late drenched with sweat. He complains of general sluggishness of body and of mind. He does not grasp questions readily and cannot remember as well as he used to, probably because memories are not registered. He cannot, of course, remember a question the meaning of which he did not grasp. His memory impairment, then, we may fairly conclude, is not due to a cortical atrophy, but rather to a dulling of the cortex, so that it does not readily register the various sensory impulses; and there is a "let down" in his general condition which is not found in mere biliary tract disturbances or gastric ulcers. Whatever the ultimate diagnosis is to be, it must satisfactorily account for this important symptom of asthenia.

So far as our observations of the patient are concerned, while he has been with us in the hospital he has been wholly without fever. Hence the diagnosis ought to be that of a condition not continuously, but rather intermittently, associated with the febrile state. He entered Mercy Hospital on the 21st of January. On only one occasion since that time has his temperature gone as high as 99.4° F.; on two occasions it has reached 99° F., and all the rest of the time it has been normal or subnormal. One must then conclude that the pathologic process is a mild infection of

some sort, chronic in type, capable of giving rise to only a slight degree of very intermittent fever.

Such temperature and weakness might be associated with disease of the thyroid gland. In ordinary hyperthyroidism the weakness is very considerable and fever is a most frequent symptom. Asthenia is also very characteristic of other diseases of the ductless glands, particularly of Addison's disease, in which it is a cardinal symptom. In pancreatitis asthenia is very marked, and in that disease of the pancreas known as diabetes mellitus asthenia is a crucial symptom. In all cases of anemia weakness is a prominent symptom. Is not this patient's asthenia due to anemia? It does not seem altogether probable that this question should be answered affirmatively without reservation, for his pallor, though perfectly evident, is not the extreme pallor associated with great physical weakness. His asthenia is not associated with dyspnea, and consequently it is not a cardiac asthenia. His asthenia is, however, associated with drenching night-sweats and other signs of vasomotor paresis. Therefore, taking into consideration the vasomotor paresis indicated by his sweating at night without signs of any high degree of infection, one might infer that the pathologic process at work, whatever it is, is one which is more apt to be associated with disease of the ductless glands and an impaired blood state than with a cardiac or any other form of asthenia.

On examining him we find quite a number of interesting points. In the first place, there is no tenderness over the liver at the right hypochondrium and no tenderness on deep percussion over the gall-bladder. There is no tenderness or enlargement of the spleen, no tenderness over the duodenal area, no tenderness over the appendix. There is, however, some tenderness at times over the right and left iliac fossæ of a vague sort. There is no tenderness over the pancreas and no ascites. These negative findings today are suggestive of no present activity on the part either of a gastric ulcer or of an inflamed gall-bladder.

On examining his lymphatic glands we find some slight enlargement of the glands at some places. In the right groin the glands are considerably larger than they should be, and there is

some enlargement of the right and left cervical glands. The left inguinal glands are about as they should be and so are the axillary glands. From these findings one might infer the possibility of lues, because that disease may at times present just such slight glandular enlargements, but in a luetic infection not only are the inguinal glands affected, but the majority of glands are slightly enlarged, especially glands which usually escape enlargement in other diseases, such as the epitrochlear glands, the posterior cervical glands, and the glands about the saphenous opening. These glands begin to enlarge shortly after the initial lesion and they usually remain large for at least five years or more.

Examination of his bones shows tenderness of the sternum; he has no soreness in the shin bones, but occasionally there has been tenderness in the thigh bones. Today he is especially tender over the sternum.

Now there is another interesting phenomenon in his case, and that is a complaint of the reduction of his sensitiveness to sound. He does not hear so well as he did formerly, and this symptom, taken in connection with other things, becomes of some importance. You will remember that certain blood states, the leukemias and pseudoleukemias, are often associated with such deafness. So one wonders whether the deafness may be so explained in this case, particularly also because of this tenderness in the sternum.

When we inquire into the hemorrhages that sometimes occur in perverted blood states we find that he has had nose-bleed occasionally during the past year, but never before. These nose-bleeds have all been spontaneous, and such hemorrhages are, of course, a matter of inquiry whenever they are met with. It is evident that the contemplation of the symptomatology of such a case as this will necessarily drive us straight to the examination of the blood. I may say, however, that the patient came into the hospital believing that his was an abdominal case, and with the expectation of an operation.

If you will all look at this slide with a high-power lens it will not take two moments to make the diagnosis (demonstrating slide under microscope). The first blood examination, which

was made two days after his entrance, showed a count of 3,190,000 red cells and 232,000 white cells; and a differential white count gave lymphocytes 6 per cent., polymorphonuclear cells 31 per cent., eosinophils 2 per cent., basophils 4 per cent., myelocytes 57 per cent.—a myelogenous leukemia. Another count, made on the 27th, showed 235,200 white cells; a count on the 28th gave 233,800, and one on the 30th, 242,000.

The urinalysis showed no albumin, sugar, casts, or red blood-cells; the specific gravity was 1020; there were five to ten white cells per field.

There is, then, with the examination of the blood a complete explanation of the unusual symptoms of which he has complained, with the exception of certain abdominal symptoms which might well be due to an associated cholecystitis, which, indeed, might even stand in some predisposing relation to the disease of the blood-making organs. The thing that makes the case unusual is that in a myelogenous leukemia we do not ordinarily expect to find such abdominal symptoms, but occasionally abdominal pains become of great value to a patient because they demand medical attention. It was the pain which brought him to the doctor; he could endure his weakness, but he could not endure his pain.

Now as to the heart: he has a very slight systolic murmur at the apex of the heart, with a reduplication of the apical second sound, also a systolic murmur over the pulmonary area, but there is nothing abnormal over the aortic or tricuspid areas. This constitutes a set of findings very characteristic of a case of chlorotic anemia. He has, of course, with his leukemia a large reduction of his red blood-cells and a reduction in his hemoglobin of equal extent, so that the picture is one of chlorotic anemia. It is not at all strange, therefore, that he should show the cardiac findings which we meet with in a young girl suffering from chlorosis, namely, a slight systolic murmur at the apex not transmitted to the axilla, and a louder systolic murmur best heard over the base of the heart.

It is a very interesting thing that there has been discovered by a pure accident a new remedy in the treatment of leukemia.

The observation was made in the service of Dr. Llewellys F. Barker, of Johns Hopkins Hospital. It was noticed that in cases of poisoning from benzin in young girls there was a marked leukopenia. If intoxication with benzin could have such an effect upon the numbers of the white cells, it was a fair inference that it might be possible to reduce the number of leukocytes in the various leukemias by giving benzin, and the experiment was accordingly made. At first the new treatment was hailed as a great discovery, and benzin was enthusiastically given in leukemic cases all over the country. The method of administration was to give 5 or 10 minims three times daily, increasing the amount gradually until 30 or 40 drops were given three times daily. Special care was taken to make sure that a refined product was given, a chemically pure form. Adverse reports multiplied, until the remedy fell into absolute ill-repute.

Was not the error made of giving a refined product? It was the crude article which caused the symptoms. We have in this hospital a patient with splenic leukemia whose spleen was so large that it extended down 3 inches below his navel. He was running, as this patient is, between 200,000 and 300,000 leukocytes per cubic centimeter. He has been here for a year, and during this time has been on two kinds of treatment: he has taken the refined benzin and he has taken the commercial benzin. He did not improve on the refined benzin, but on the common, unrefined he grew very much better. Perhaps there is something in commercial benzin which is taken out with the process of refinement, and which is an active constituent in the treatment of these cases. He has run up his dose to 70 drops three times a day. Formerly it was not thought that such large doses could be tolerated, but this patient has voluntarily taken them, with the result that he is symptomatically cured. His strength seems to me to be excellent, the spleen is only slightly enlarged, and although the blood still shows an increase in the number of white cells to about 30,000 per cubic centimeter, as contrasted with the former findings of 200,000, his strength and sense of well-being are so much improved that he is able to carry on his work in the hospital. Possibly the improvement is a remission natural to the disease.

More therapeutic experiments must be made. His is a degree of improvement which has not been attained hitherto in these cases.

These patients usually become more and more anemic and eventually go on to death from asthenia. This young man is just in the beginning of his trouble; he has probably been having it for only a year. It evidently was not there four years ago when he had malaria in Cuba or it would have been discovered when his blood was examined.

This case is another demonstration of the value of routine work. Suppose he had been taken into a hospital where blood examinations are not done as a routine. There was nothing in his case at first glance demanding a white count. He would have had his abdomen opened. If his blood had not been examined here he would have been operated upon, for he came in for that purpose. Blood examinations should be made in all cases, and since they were made in this case it was impossible to escape making a diagnosis of myelogenous leukemia.

This patient is already upon the benzin treatment. We have ordered a Wassermann, but the report is not in as yet. [*Note.*—It was negative.] If it turns out to be positive, of course he should be treated very intensively with the antispecific treatment. If it turns out negative the thing to do will be to push the benzin to the limit. [*Note.*—The patient returned in ten days to his home-physician, who promised to continue the treatment, but we have not heard from him.]

CLINIC OF DR. ARTHUR F. BEIFELD

COOK COUNTY HOSPITAL

DIFFERENTIAL DIAGNOSIS OF A CASE WITH AN ENORMOUS NUMBER OF NUCLEATED RED CELLS IN THE CIRCULATING BLOOD

(With a note by DR. A. B. KANAVEL on the Indications for Splenectomy.)

Technic of Blood Examination. Definition of Basophilic Granulation, Polychromasia, etc. Significance of Megaloblasts.

Four Conditions Associated with an Enormous Number of Erythroblasts in the Blood: (1) Pernicious Anemia (Blood Crises); (2) Chronic Myeloid Leukemia; (3) Anemia Pseudoleukemica Infantum; (4) Carcinomatosis of the Bone-marrow.

Present Status of Splenectomy in Pernicious Anemia, Hemolytic Icterus, Splenic Anemia, Banti's Disease, and Other Forms of Splenomegaly.

DR. BEIFELD: Instead of beginning the study of our patient in the usual manner, let us postpone for the time being the history and the results of the physical examination, and build up our case, as far as is possible, on the basis of the hematologic findings. I will ask you, therefore, to look at the slide under the microscope and to tell me what diagnostic conclusions you would draw from the blood-picture.

Technic of Staining Blood-smears.—While Dr. K. is busy, it might not be amiss to say a word or two relative to the staining of blood-smears. As you know, there are many available methods. Some are particularly suitable for one purpose, some for another. The tri-acid stain, for example, is especially valuable for the identification of ripe neutrophilic granules, such as we see in the poly-

morphonuclear leukocytes; on the other hand, it fails to show basophilic granulation of the red cells. Again, if one wishes to study nuclear structure, the Giemsa or the combined Jenner-Giemsa stain is preferable.

What we are interested in, however, is a method which is rapid, more or less uniformly successful, and which will show the majority of features essential to a diagnosis. The stains of Leishman, Jenner, Giemsa, and Wright fall into this category. For routine work I employ the Wright stain almost exclusively. The technic is extremely simple, and the time required for an almost uniformly successful preparation is less than ten minutes.

Wright's stain, ready for use, may be purchased at almost any medical supply house, and, when obtained from a reliable source, gives fairly constant results. It is much more satisfactory, however, to prepare one's own stain by using the compressed tablets found on the market.[1] One of these tablets dissolved in 10 c.c. of chemically pure methyl alcohol[2] yields the correct concentration. The cover-glass or slide preparation, resting upon a level non-absorbing surface—glass, wood, or rubber—is first covered with the stain, which is allowed to act, on the average, one and three-quarter minutes. You will quickly become familiar with your particular stain and discover whether the optimum is one and one-half, one and three-quarter, or two minutes. The staining is to be done by the watch. The next step is the addition of *distilled* water. The admonition to add water only until a fluorescent scum appears has always seemed to me superfluous. It is my custom to add water until the preparation seems about to overflow—a little experience will teach you when that point has been reached—to draw the diluted stain into a medicine-dropper several times in order to obtain a good mixture, and to allow the differentiating process to continue seven to eight minutes. Here also practice determines the correct period for the particular stain. The preparation is now washed off in tap-water, dried, and, if on a cover-glass, mounted in neutral Canada balsam.

As I have already said, this process consumes ten minutes

[1] Burroughs-Wellcome compressed tablets of Grübler's stain.

[2] American products are generally satisfactory.

at the most and yields a uniform slide showing practically all of the details necessary to a diagnosis. The preparation at which Dr. K. has been looking was stained by this method with no unusual care, and, as you will concede when you examine it later, is as good for routine work as one could wish.

After this digression, I will ask Dr. K. what he has found.

Dr. K.: I have noticed, in the first place, that the red blood-corpuscles seem considerably below the normal in number; I should judge that the count is about 2,000,000. Second, in almost every field (Leitz, oil immersion, $\frac{1}{2}$) there are one or more red cells which I think are nucleated. Many of these are about normal in size, while some are considerably larger than normal. The nuclei of some of these cells are round, a number are composed of two round portions, while many have a clover-leaf design. One nucleus, I believe, was undergoing mitosis.

I saw, also, hundreds of red cells containing bluish granules —basophilic degeneration. The leukocytes seem to be about normal in number; the lymphocytes, however, appear relatively increased at the expense of the polynuclear neutrophils.

Dr. Beifeld: A very excellent summary of conditions. An oligocythemia is present—the last enumeration shows 1,800,000 red cells; nucleation is a striking feature, the nuclei having, among other things, the features already mentioned; the white corpuscles are within the limits of the normal—the count is 8000 and the presence of innumerable red cells containing basophilic granules is a very striking feature. Relative to this last, however, allow me to say that the term "basophilic degeneration" is not a good one—"basophilic granulation" is preferable. The reason for this will appear a little later. And, finally, as was noted, there is a slight relative lymphocytosis, the actual percentage being 40 for the lymphocytes and 50 for the polynuclear neutrophils.

With due credit to Dr. K., I must add that he has failed to mention a great many very important details shown by this preparation. First of all, there is present a high grade of anisocytosis; that is, the red blood-corpuscles differ greatly in size. Only a minority are perfectly normal in this respect, a large number being considerably smaller than the normocyte, while the

bulk of the red cells are noticeably larger than the average normal cell. We have to do, in other words, with a megalocytic picture. Another striking feature is the presence of large numbers of deformed cells, a condition called poikilocytosis. The variations in shape which the red cells may undergo are well known to you and need not be discussed at this time.

Fig. 62.—Microphotograph showing four nucleated red blood-cells in one field. This average per field (magnification 650) is only slightly in excess of that prevailing throughout the remainder of the specimen. Nucleated cells all of the normoblastic type. Nucleus of cell in upper left corner illustrates the characteristic spoke-like arrangement of the chromatin. Nuclei of other cells undergoing karyorrhexis.

If I focus carefully I can see a color change other than basophilic granulation in many of the erythrocytes, namely, a more or less even admixture of blue. This phenomenon is called polychromasia, and as it has the same significance as the granulation I shall discuss the two together later.

A word now as to the nucleated red cells which are present in the ratio of 60 to 100 white cells. The majority are normoblasts, or cells of about normal size. It must be emphasized, however,

that the size of a nucleated red cell is not the only criterion of its type. The character of the nucleus is more important in determining whether a given cell is a normoblast or a megaloblast. The typical normoblastic nucleus is generally round, and the chromatin network, which is coarse, is arranged more or less after the fashion of the spokes of a wheel (Fig. 62). The specimen from our case shows these characteristics in exquisite fashion. It shows also most of the variations from the typical seen in

Fig. 63.—Microphotograph (magnification 1200) showing a normoblast (upper left; nuclear structure not clear) and a Cabot ring body (probably a nuclear remnant). Several cells contain basophilic granules.

normoblasts. Thus we observe densely staining nuclei with no hint of a spoke arrangement, a condition known as pyknosis; also cells with several round or nearly round nuclei; cells with only nuclear detritus; and, finally, nuclei which have been extruded from the cell body (Figs. 63 and 64).

The megaloblast, it is true, is, as a rule, larger than the normoblast, but its nucleus is itself diagnostic. Instead of the coarse radiating rods of chromatin, we see a delicate network, with no definite arrangement, and taking a much lighter strain than the

normoblast. In the slide before you, though there are many megaloblasts, they are far less numerous than the normoblasts. The actual ratio is 7 to 1. Between the normoblast and megaloblast is another erythroblast having some of the characteristics of both, and which we call a mesoblast. These are also present here in considerable numbers, and in the count have been included in the megaloblasts.

Fig. 64.—Microphotograph showing a megaloblast (below) undergoing mitosis. The basophilic granules in this cell are plainly seen. (The cytoplasm is also distinctly polychromatic in the stained specimen.) The megalocytic picture is clearly evident here. Above, a polynuclear neutrophil. (Magnification 1200.)

Finally, before concluding the subject of the nucleated red cells, I wish to call your attention to the fact that a great many of them show one or both of the changes already mentioned in connection with non-nucleated erythrocytes, namely, polychromasia or basophilic granulation (Fig. 64).

There are still other important features of this blood slide to be commented upon. One of these is the amount of hemoglobin per cell. Though there are fewer than 2,000,000 red cells per cubic millimeter, you will observe that the individual cell stains more or less uniformly, many, indeed, more deeply than does a

normal cell, and quite differently from the average cell, say of a secondary anemia, or of a chlorosis, in which only a narrow rim of protoplasm can be seen. In other words, there is a relative increase of hemoglobin per unit volume of red cells. The estimation of the color index confirms this. The hemoglobin by the Sahli apparatus registers 45, which, with 1,800,000 red cells, gives a color index of 1.2.

The importance of the blood-platelets in certain conditions is frequently not given sufficient emphasis. These bodies are well shown by the Wright stain. In this specimen one must look for a considerable time before finding a group of platelets, indicating that they are considerably diminished in number.

Let us now recapitulate what we have found in the form of a tabular outline which will facilitate our discussion of the diagnostic possibilities:

The Red Blood-corpuscles:

Number, 1,800,000.

Hemoglobin, 45.

Color index, 1.2.

Size.—Few of normal size; many smaller than normal; the majority larger than normal. Also many gigantocytes.

Shape.—Marked poikilocytosis.

Staining Characteristics.—Basophilic granulation and polychromasia common both in nucleated and non-nucleated cells.

Nucleation.—Enormous numbers of nucleated cells, normoblasts of various types considerably outnumbering megaloblasts. The proportion of nucleated red cells to leukocytes is as 6 : 10. On the basis of a leukocyte count of 8000 this would mean 4800 nucleated red cells per cubic millimeter.

The White Blood-corpuscles:

Number, 8000.

Differential count:

Polynuclear neutrophils	50 per cent.
Lymphocytes	40 " "
Large mononuclear and transitional cells	5 " "
Polynuclear eosinophils	3 " "
Polynuclear basophils	0
Myelocytes (neutrophilic)	1 " "
Turk's "irritation forms"	1 " "

The Blood-platelets:

Considerably reduced in number.

With this information before you, Dr. K., what is your presumptive diagnosis?

Dr. K.: I should not care to make a diagnosis from the blood alone—that is, without the history and physical findings—but if I had only this slide to depend upon I should say the case is one of pernicious anemia.

Dr. Beifeld: You are quite right in saying that one ought to have before him all the evidence possible before attempting a diagnosis. A great deal, however, can be told simply from a careful examination of the blood-smear. Indeed, after a little experience you will find that even the fresh, unstained specimen will often be sufficient to enable you to make a probable diagnosis of certain hematologic conditions. Take pernicious anemia, for instance. The unstained smear will show the diminution in the number of erythrocytes, the megalocytosis, the relative increase in the amount of hemoglobin per cell, the poikilocytosis, and the leukopenia with a relative lymphocytosis; while the trained eye, after a careful search, may find a megaloblast or two. This combination of hematologic findings, though not pathognomonic of pernicious anemia, is only exceptionally found in any other condition.

This being the case, we will postpone a while longer the anamnesis and physical findings, and analyze the blood-picture. You have said that you favor the diagnosis of pernicious anemia, Dr. K. Is there anything in this table not consistent with that diagnosis?

Dr. K.: The only inconsistent thing that I can see is the absence of a leukopenia. But this may be due to some complicating infection. Has the patient a temperature?

Dr. Beifeld: Your points are all well taken. The white count of 8000 does not harmonize with the usual picture of a pernicious anemia; and, as a matter of fact, the patient is running a low degree of fever. But what about the tremendous number of nucleated red cells; is that common in pernicious anemia?

Dr. K.: I believe that large numbers may be found in what are called the *blood crises* of pernicious anemia.

Dr. Beifeld: Yes, in some cases of pernicious anemia—per-

haps in all, if frequent enough examinations were made upon which to base conclusions—enormous numbers of erythroblasts are thrown into the circulation, indicating a tremendous activity of the bone-marrow. In the average case, however—and this is very important for you to know—nucleated red cells, chiefly megaloblasts, are found only sparingly. One may have to look through many slides before finding a single megaloblast, and not only is it necessary to look carefully for these cells on one day, but on many days, if the first search is not successful.

This leads us to another important point, namely, that the diagnosis of an aplastic anemia is permissible only when repeated examinations over a long period of time show that nucleated red cells are absent, and that the bone-marrow does not respond to calls for greater activity. Even then we are not infrequently surprised at autopsy to find that a case assumed to have been of the aplastic type exhibits a red marrow in the long bones.

This discussion opens still another phase of the nucleation question, and that is, *the significance of the megaloblast in pernicious anemia*. It is quite true that megaloblasts are found in other conditions which we shall consider in a few minutes. In these other conditions, however, there are also present normoblasts in large numbers. This may be the case, it is true, in the blood crises of pernicious anemia, and it is just here that the presence of megaloblasts has the least diagnostic significance. It is in those cases of pernicious anemia in which a few nucleated red cells, almost exclusively of the megaloblastic type, are found after long, careful, and repeated search that the diagnosis of idiopathic anemia gains immensely in strength. This is the great significance of the megaloblast in pernicious anemia.

Now, Dr. K., I should like you to develop the diagnosis in this case about its most striking feature, which is the presence of erythroblasts, chiefly of the normoblastic character, in tremendous numbers. You have mentioned the fact that the blood crises of pernicious anemia may show this picture. What other conditions must we consider in the differential diagnosis?

Dr. K.: Leukemia would have to be considered, although the low leukocyte count would rule that out.

Dr. Beifeld: Your first suggestion is a good one, but your conclusion is not entirely correct. Myelogenous or myeloid leukemia—the chronic form—is one of the conditions in which there is found at almost all times a large number of nucleated red cells. Normoblasts outnumber megaloblasts, just as in our case. There is no hematologic condition, with the possible exception of the von Jaksch type of anemia, in which one can constantly find so great a variety of pathologic blood-corpuscles, both red and white. This is a point it will be well worth your while to bear in mind, especially those of you who may do medical teaching at some future time. A blood slide from a case of chronic myeloid leukemia is of almost unlimited value in the possibilities it offers of exhibiting abnormal blood-cells.

Leukemia, therefore, must be considered in the diagnosis so far as nucleation is concerned. Nor does the fact that there are only 8000 white cells militate against this diagnosis. All cases of anatomically proved myeloid leukemia do not show *intra vitam* the characteristic blood-picture in which are found 100,000 white cells or upward. The real test of a leukemia of any kind, acute or chronic, is, in addition to the blood findings, the histologic examination of the organs—bone-marrow, spleen, liver, lymph-nodes, kidneys, etc. Thorough examinations of this sort have shown almost beyond a doubt that a true myeloid leukemia may be present with fewer than 80,000 leukocytes per cubic centimeter—the upper limit usually set for a leukocytosis—in the circulating blood. Cases showing ill-defined limits of 20,000 to 80,000 white cells per cubic centimeter are called *subleukemic*, or *submyelemic* in the case of myeloid leukemia; while those with a practically normal white count are called *aleukemic* or *amyelemic*. Examples of the latter, exhibiting clinically a large spleen and some lymph-node enlargement, were formerly catalogued as splenic forms of pseudoleukemia. Many of these were undoubtedly true examples of myeloid leukemia with characteristic myeloid infiltration of the organs.

The real clinical test of subleukemic and aleukemic leukemias, therefore, is not the total number of leukocytes in the unit volume of blood, but the character of the cells present. The determining

type in all chronic myeloid leukemias is the myelocyte, the neutrophilic form of which usually predominates, though the eosinophilic and basophilic varieties are present in considerable numbers. We can rule out the diagnosis of chronic myeloid leukemia in our case without great difficulty, in view of the fact that the percentage of myelocytes is only 1. The physical examination, furthermore, reveals only a slight enlargement of the spleen, the edge being just palpable below the costal margin.

The third condition that must be considered because of the enormous number of nucleated red cells present is von Jaksch's anemia or *anemia pseudoleukemica infantum*. The differentiation here is not difficult, as the chief point of resemblance is the occurrence in both of many nucleated red blood-cells. The von Jaksch type of anemia, however, as its name implies, occurs exclusively in infancy, and is associated with a marked splenomegaly and a pronounced leukocytosis.

The fourth and last condition that must be considered is one that has many points in common with pernicious anemia and is often mistaken for the latter. This is *carcinomatosis of the bone-marrow*. The age incidence is the same as in pernicious anemia; poikilocytosis may be marked; anisocytosis is usually prominent, and the megalocyte may be the predominating cell; basophilic granulation and polychromasia are common; and the color index is not infrequently greater than 1. The striking feature, hematologically, of carcinomatosis is the tremendous number of nucleated red cells, and, just as in the case before us, the predominating cell is the normoblast.

The blood-pictures of pernicious anemia and bone-marrow carcinoma differ, however, in several very important details. In carcinoma the flooding of the circulating blood with nucleated red cells is a *constant* feature, not periodic as in the crises of pernicious anemia. A leukocytosis of 20,000 to 30,000, furthermore, is characteristic of carcinoma which has invaded the bone-marrow. And, finally, the blood-platelets show a marked increase in the malignant condition in contrast with their almost complete absence in pernicious anemia.

The clinical side of our case, furthermore, is not consistent

with the assumption of a malignancy with metastases in the bone-marrow. Malignant new growths of four organs in particular—thyroid, breast, prostate, and adrenal glands (hypernephroma)—tend to produce metastases in the bones. Careful examination of our patient fails to reveal any abnormality of the thyroid gland or of the breasts, and there is not the slightest indication of the presence of a hypernephroma. Nor is there evidence of a malignant growth of any organ other than those mentioned. Speaking against malignancy, furthermore, are the following facts:

The patient has been troubled intermittently for three years with the symptoms which brought her to this hospital two months ago, and in these three years she has lost only 10 pounds in weight, which hardly harmonizes with the assumption of a malignancy.

Of the four conditions which may be associated with an enormous erythroblastemia, chronic myeloid leukemia, von Jaksch anemia, and bone-marrow carcinomatosis are obviously not further to be considered in the differential diagnosis, although the blood-picture varies in certain particulars from what we are accustomed to call the average in pernicious anemia. The large number of nucleated red cells we have noted may be indicative of a blood crisis, but the presence of 8000 white cells, and the fact that normoblasts are more numerous than megaloblasts, are not consistent with this same average picture.

Let us turn for a moment from the consideration of the hematologic aspects of the case, and see what information can be derived from the history and physical findings.

Present History.—Our patient is forty-eight years old, American born, married, and a seamstress by occupation. As has already been mentioned, she entered the hospital two months ago. Upon admission she complained of the following symptoms: Weakness, a tendency to become tired very quickly, dizziness, ringing in the ears, shortness of breath, loss of appetite, palpitation of the heart, swelling of the legs, insomnia, and, as she terms it, indigestion.

The patient's previous history indicates that this is not the

first attack of her trouble. Her illness began, it would seem, a little less than three years ago with symptoms not unlike the present ones, though perhaps less severe. At that time she was a patient in a hospital in California, and after a period of treatment lasting about three months she was discharged apparently as well as ever. She does not know the diagnosis of her condition made at that time. Nine months later there occurred a similar attack, also lasting two months, and yielding well to treatment. Twelve months after this second illness she again was forced to give up her work because of increasing weakness, and this time she was confined to her room for three months before she felt able to resume her occupation.

From the third attack to the present, the fourth, though she has been able to work almost every day, she has not felt strong, and has continued sewing only because necessity demanded it. Two months ago, however, the above-mentioned train of symptoms finally became so severe as to force her to apply for admission to a hospital, and she has been in this institution since.

Aside from this recurrent illness, the patient has always been well. The family history throws no light upon her condition. She is the mother of three healthy children and has had no miscarriages. There is no alcoholic history. We have already noted that the patient has fever. This is of a low-grade type, rarely exceeding 101° F. You will see from the chart that the temperature-curve follows no type and that for days at a time she is afebrile.

Physical Examination.—As you will observe, the patient is fairly well nourished, the subcutaneous fat being well preserved. To be exact, she weighs 140 pounds now as compared with 150 pounds, her weight for a number of years preceding the onset of her sickness three years ago. Upon cursory examination you would perhaps say that she is jaundiced, but, as a matter of fact, though the conjunctivæ are of a subicteric tint, the color of the skin might be more correctly described as lemon yellow. Contrasting with this color is the distinct pallor of the tongue and lips.

Observing the skin more in detail, we note scattered irregular

patches of brownish pigmentation, chiefly on the chest, abdomen, and back, while here, on the right arm, on the abdomen, and on the left leg are pin-head-sized reddish spots which do not disappear upon pressure and are evidently petechial hemorrhages. There is present also a slight, bilateral malleolar edema. Enlarged lymph-nodes are not palpable.

The pupils are equal, regular, and respond promptly to light and accommodation. The ophthalmoscopic examination, however, reveals an interesting finding, namely, a retinal hemorrhage the size of a large pin-head in the right fundus. The mouth, aside from the extreme anemia of the mucosa and the presence of scattered pin-point hemorrhages on the hard palate, shows no changes. The teeth appear to be in very fair condition and, as a matter of fact, *x*-ray examination reveals no pus pockets or bone absorption about the roots.

You can easily see the marked heaving of the vessels of the neck. On the right side there is a loud humming-top murmur. Aside from the signs of a slight emphysema the lungs are negative. The heart is somewhat dilated, the limits of deep dulness extending from a point 1 cm. to the right of the right sternal edge to the constructed mamillary line on the left side, the base being at the third rib. Palpation is negative, and auscultation reveals only a soft systolic blow over the pulmonic area. The vessels are soft and the pulse rapid and compressible. The pulse-rate during the patient's stay in the hospital has been constantly rapid, varying from 85 to 120. The blood-pressure, when last determined, was 100 systolic and 80 diastolic.

The edge of the liver can be felt about 5 cm. below the costal arch and is rounded. The surface of the organ is smooth, and its consistency is certainly not increased over the normal. The spleen, as previously remarked, can just be felt on deep inspiration, while percussion shows a moderate enlargement upward. Otherwise the abdomen appears to be normal.

Examination of the nervous system reveals no anomalies except the absence of the knee-jerks. The various forms of sensation are normal and there are no pathologic reflexes.

Laboratory Findings.—A few words, finally, as to the labor-

atory findings, and we shall be ready to resume the consideration of the diagnosis of this case. The urine has from time to time shown a trace of albumin and a hyaline cast or two. A striking feature of the urine, however, has been the constant presence of a marked Ehrlich aldehyd reaction, indicative of urobilinogen. We cannot enter into the question of the formation of this body nor of its significance further than to say that it points to a disordered liver function.

Repeated examinations of the stool showed no parasitic ova and also no blood. The Wassermann reaction, both with the patient's blood and with her spinal fluid, was negative. The various globulin reactions—Noguchi, Nonne-Apelt, and Ross-Jones—were also negative. Analysis of the gastric content revealed a complete absence of free hydrochloric acid.

Previous examinations of the blood have differed in several important particulars from the data obtained from the smear under the microscope. A slide prepared soon after her entrance into the hospital—*i. e.*, two months ago—showed the following:

Erythrocytes	1,200,000
Hemoglobin	30 (Sahli).
Color index	1.25
Leukocytes	2800
Polynuclear:	
Neutrophils	44 per cent.
Lymphocytes	53
Large mononuclear and transitional cells	2
Eosinophils	0.5
Basophils	0.5
Myelocytes	1.0
Anisocytosis	Marked, large cells predominating.
Poikilocytosis	Marked.
Polychromasia	None.
Basophilic granulation	Absent.
Nucleated red cells	One megaloblast found after prolonged search.
Blood-platelets	Practically absent.

One month after the patient had entered the hospital she felt symptomatically a great deal better, and the blood-picture had undergone the following changes:

Erythrocytes	1,500,000
Hemoglobin	35
Color index	1.17
Leukocytes	4000
Polynuclear neutrophils	48 per cent.
Lymphocytes	48 " "
Large mononuclear and transitional cells	2
Eosinophils	0.5
Basophils	0.5
Turk's irritation forms	0.5
Myelocytes	0.5
Anisocytosis	Marked, megalocytic type.
Poikilocytosis	Marked.
Polychromasia	Considerable.
Basophilic granulation	Considerable.
Nucleated red cells	One megaloblast per hundred white cells counted.
Blood-platelets	Practically absent.

Diagnosis.—We are ready now to return to the consideration of the diagnosis. Before our digression we were able to say, without much fear of dispute, that three of the conditions which are associated with a marked red cell nucleation—chronic myeloid leukemia, anemia pseudoleukemica infantum, and carcinomatosis of the bone-marrow—were readily eliminated as possibilities. There remained only pernicious anemia, which fitted well into the picture except for a few hematologic details. But now we need have no hesitation in making a definitive diagnosis of pernicious anemia with the following additional information before us. The age of the patient, the symptom complex, the lemon yellow color of the skin, the very moderate loss of weight considering the duration of the illness, the *remissions* in the sickness, the retinal hemorrhage, the urobilinuria, the petechial hemorrhages of the skin and hard palate, the pigmentation of the skin, the absence of free acid in the stomach contents, the loss of the knee-jerks, indicating cord changes, and, finally, blood-pictures on two previous occasions entirely characteristic of pernicious anemia.

Variations in the Blood-picture of Pernicious Anemia.—It is obvious, therefore, and this is one of the prime reasons for presenting this case, that in pernicious anemia the blood varies considerably, depending upon the phase of the disease. A knowledge

of this fact will enable you not only to reconcile with the diagnosis of pernicious anemia hematologic details which do not belong to the so-called average picture, but to determine at a given time the exact condition of the patient, whether it be on the up-grade, on the down-grade, in its terminal phase, or as showing the characteristics of an intermission.

In order to enable you to carry this away in a compact form I shall place upon the board a table which I have taken from Naegeli's "Blutkrankheiten und Blutdiagnostik":

1. Commonest picture.	2. Periods of greatest severity.	3. Rapid improvement.	4. Gradual improvement.
Intermingling of periods of improvement and decline.	Especially preagonal.		
Polychromasia common.	Polychromasia rare and finally 0.	Polychromasia common.	Polychromasia common, but gradually diminishing.
Basophilic granules present, generally not marked.	Basophilic granules rare and finally 0.	Basophilic granules increasing.	Granulation common, constantly decreasing.
Nucleated reds a few.	Nucleated reds rare or 0, may be abundant just before death.	Nucleated reds very common (blood crises).	Nucleated reds steadily diminishing.
Leukocytes average 2000–4000.	Leukocytes enormously reduced.	Transitory moderate leukocytosis (8–15,000).	Gradual increase 3 to 4–6000.
Polynuclears (neutrophils) average 1000–2000 per cubic centimeter.	Neutrophils markedly reduced, often to 500–100 per cubic centimeter.	Neutrophils greatly increased.	Neutrophils steadily increasing from 2 to 4–6000.
Large monos and transitional reduced.	Monos reduced to 0.	Monos greatly increased.	Monos increasing from 1 to 4–7 per cent.
Eosinophils generally 1 to 2 per cent.	Eosinophils 0.	Eosinophils increased.	Eosinophils 2 to 5 per cent. and more.
Lymphocytes 50 per cent. and more.	Lymphocytes 70 per cent. and more.	Lymphocytes markedly reduced.	Lymphocyte per cent. gradually decreasing from 60 to 40 to 20.

The red blood-corpuscles and the hemoglobin are increased in the periods of improvement in such a way that the amount of pigment per corpuscle remains greater than in the normal cell; *i. e.*, the color-index continues to be greater than 1.

The foregoing table includes perhaps the greater number of the variations which the blood-picture of pernicious anemia undergoes in its different phases. It is not at all infrequent, however, to meet with pictures which are intermediate and do not exactly fall into any of these groups. In these cases frequent examinations of the blood will show in what direction things are going.

When a remission is well established the blood-slide may show only slight, if any, variations from the normal. It must be emphasized, however, that a complete subsidence of the subjective features and a perfect restoration of the patient's working ability do not by any means signify that the blood has returned even in any great degree to its normal condition. There may be a clinical remission, for example, with 3,000,000 red cells per cubic centimeter. In the great majority of cases, however closely the erythrocytes approach the normal, the volume percentage of hemoglobin continues relatively high; that is, the color-index remains above 1. In some instances, furthermore, anisocytosis practically disappears, though the rule is for a cell somewhat larger than the normocyte to predominate. There may remain little or no poikilocytosis. The completer the remission, the more closely do the leukocytes, both in the number per cubic centimeter and in their percental relations, approach normal conditions.

You will see, therefore, that in the average remission, just as in the other phases of pernicious anemia, the blood-picture tends to retain its most distinguishing feature, namely, the embryonic type of blood formation. A small minority of cases may, in the well-marked remission, exhibit nothing which warrants a diagnosis of pernicious anemia.

Our patient entered the hospital in a condition of moderate severity, which has persisted with no great change until recently, when there began a period of rapid improvement. Hematologically, improvement in pernicious anemia is synonymous with a re-

newed activity of the bone-marrow, and is evidenced by a throwing into the blood-stream of bone-marrow elements. Indicative of this is the increase in the number of red cells, the increase in the total number of leukocytes, and in the percental displacement of lymphocytes by granular cells, *i. e.*, polynuclears, chiefly neutrophilic; in a more or less rapid increase in the number of nucleated red cells in the blood (normoblasts generally predominating in the most active periods), and in the prevalence of polychromasia and basophilic granulation. The latter is regarded by some as an evidence purely of degeneration, by others as indicative of both degeneration and regeneration; and, by still others, as meaning only regeneration. This last view is held by probably the majority of observers. It is for this reason that I condemned the use of the term "basophilic degeneration" earlier in the clinic.

Throughout these various stages and blood changes—and this has already been emphasized—one feature remains constant in nearly every case, namely, the blood-picture as a whole retains its embryonal character. It is still an unsettled question whether the blood assumes the embryonic type because of the exhaustion of the bone-marrow, *i. e.*, foci of blood formation active in fetal life are called upon to make good the medullary insufficiency, or whether the active factor concerned in the causation of pernicious anemia leads inherently to the production of this type of erythropoiesis.

There remain still many other phases of pernicious anemia that I should like to discuss with you, such as the question whether the blood-picture of the so-called secondary form is indistinguishable from that of the idiopathic type (including cases due to syphilis, Dibothriocephalus latus, and pregnancy), the pathogenesis of the disease, the remainder of the differential diagnosis, and the present status of the treatment of the condition. But these phases of the topic must be reserved for a future clinic.

However, as Dr. Kanavel's surgical clinic immediately follows, I cannot overlook this opportunity of asking him to take up with you the position of splenectomy in the treatment not only of pernicious anemia, but of those other conditions in which recently it has found so prominent a place.

DR. KANAVEL: Pernicious anemia, and particularly splenic anemia, hemolytic icterus, Banti's disease, etc., are still more or less ill-defined clinical entities, the classification of which is based upon a rather insecure pathologic and physiologic foundation. At the very outset, therefore, I may say we are as yet in no position to take a postive stand as to which types of these clinical complexes should be benefited by a removal of the spleen. There is the danger, on the one hand, of condemning the procedure because of failures in cases unwisely selected for the operation, and, on the other, of subjecting many patients to unnecessary and harmful surgery of overenthusiasm.

Until the pathogenesis of these various diseases for which splenectomy has been suggested is better understood, each case presenting itself must be made the subject of a most thorough clinical, bacteriologic, chemical, and pathologic study, both before operation is recommended and after operation if surgery is resorted to. Splenectomy as a procedure will gain in prestige in the treatment of these difficult conditions only through the effort of determining the underlying physiology and pathology of the particular case, and it is only by such intensive study that definite indications can be formulated and the procedure made a safe one.

Physiologic chemistry should find an especially fertile field in this study. Investigations along these lines would concern themselves, among other things, with the nature of cellular proteins and expressed sera of spleens, both normal and pathologic, with the factors underlying the diminished resistance of the red blood-corpuscles to hypotonic salt solutions, as is observed in many cases of hemolytic jaundice, and with the question of an internal secretion of the spleen, which, like the hormones of other ductless glands, may be poured out in excessive amount, a condition termed by Eppinger *hypersplenism*.

It is a well-established fact that the spleen is intimately concerned in the destruction of the red blood-corpuscles, but it remains to be proved whether in any of the diseases under consideration its action is merely an augmentation of its normal function due to intrinsic splenic pathology, or whether the red cells have

become abnormally fragile because of other, as yet undetermined, causes. Even though the exact position occupied by an excessive red-cell destruction in these conditions is not known, the chronic enlargement of the spleen undoubtedly plays a prominent rôle in the production of the associated anemia. In the case of acute splenic tumor, on the other hand, nothing definite has been worked out relative to accompanying blood changes.

We may conceive of a classification of chronic splenic enlargement based upon intrinsic factors (primary enlargement) and extrinsic factors (secondary factors). The former would assume that the hypertrophy is indicative of a demand upon the part of the organism for an increase in the physiologic activity of the spleen, while the second form would explain the enlargement as one due to toxic action upon the organ, the resulting splenic pathology, in turn, producing the symptom complex which brings the patient to us. In analogy with enlargements of the thyroid gland we might imagine, further, that the primary enlargement should be of value to the organism at one time and harmful at another, and that in the secondary type the destruction of the red corpuscles might become so great as to menace the life of the individual. In this latter instance splenectomy would obviously be of great benefit to the patient, provided the underlying toxic focus could simultaneously be eradicated.

Pernicious anemia, insofar as the problems of splenectomy and fragile red corpuscles are concerned, must be approached, in my opinion, in a similar manner. Thus some cases are probably related to hemolytic jaundice, being associated with an increased fragility of the erythrocytes, while others may be found to be secondary to a chronic septic focus, the location of which may or may not be discernible. In this secondary type particularly, splenectomy, when combined with the destruction of all septic foci, promises well. The literature contains a number of reports relative to cases of pernicious anemia apparently typical in nature which have recovered and have remained well for a number of years following appendectomy, and 2 such cases have come to my personal attention.

Turning now to diseases other than pernicious anemia, we

find that splenectomy has found a definite place, particularly in hemolytic icterus. The clinical picture of this condition is well-defined, though the underlying pathology needs further illumination. The results of the operation may be said to be especially brilliant in this disease—a statement based upon the records of 46 operated cases in the literature, and upon a personal case which has remained well one and one-half years after the removal of the spleen.

In splenic anemia and Banti's disease, especially in their early stages, the results of splenectomy are likewise extremely encouraging, while it is not unlikely that von Jaksch's anemia and splenomegaly of the Gaucher type are suitable for operation if the case be not too far advanced. The anemias secondary to syphilis, chronic sepsis, and malaria fall into the same category. In these cases we have to do, apparently, with an anemia resulting from a hypertrophy of the spleen, the enlargement being the consequence of a toxemia. The splenic hypertrophy is probably beneficial in limiting or destroying the primary condition, but carries with it the detrimental consequence of an abnormal destruction of the red blood-corpuscles. A nice judgment is in place here as to whether the primary infection has been eliminated and as to the advisability of splenectomy. If the splenomegaly represents merely the aftermath of an infection which has already run its course the removal of the organ will be sufficient to relieve the anemia.

We can speak with less certainty of those splenic enlargements accompanying the various cirrhoses of the liver. In those cases in which it can be shown that the causative agent has *primarily* involved the spleen benefit can be expected from operation, while in conditions in which the splenic hypertrophy is distinctly secondary to the hepatic process little good can be expected. In this connection, however, it must be emphasized that slight, and possibly primary, enlargements of the spleen may have escaped our clinical recognition. Additional surgical and postmortem experiences are needed to establish on a firm basis the indications for operation in these cases.

Summarizing the present status of splenectomy in pernicious

anemia, hemolytic icterus, splenic anemia, Banti's disease, and allied conditions, we may say that the current enthusiastic interest in and intensive study of these processes will result, in all probability, in a complete reclassification. It is obvious, therefore, that we are in no position as yet to state definitely that splenectomy is of value in one disease and not in another. It is still too early to act according to a hard-and-fast rule if we wish to avoid improper conclusions to prevent operations in poorly selected cases by those who simply swim with the tide and are not properly equipped to study each case, and to show the advisability of operation where it is indicated.

In the present state of our knowledge we may say that splenectomy finds a well-founded indication in splenic anemia, Banti's disease, anemias with splenomegaly consequent to chronic foci of infection, when the latter can be eradicated, syphilitic and malarial splenomegalies, and in hemolytic jaundice. In the splenomegalies of hepatic cirrhosis the results of operation depend upon the type and stage of the disease, general conclusions not being warranted from our present information.

In regard to pernicious anemia, finally, the available data are not sufficient to justify too sweeping deductions. It is certain, however, that many cases exhibit a rapid improvement, more rapid and pronounced than is generally seen in the periods of spontaneous remission. It is just as certain, on the other hand, that some types are not benefited permanently, while it still remains to be seen whether any cases are cured.

A fuller knowledge of the disease upon which can be based a better etiologic classification of the different forms is essential to a final judgment. Meanwhile repeated transfusions and splenectomy produce results encouraging enough to warrant the operation in carefully studied and selected cases.

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